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Original Communications.

*SOME OF THE THERAPEUTIC RELATIONS OF THE NERVOUS SYSTEM.**

BY SOLOMON SOLIS-COHEN, M.D.†

THERE is hardly any subject in the whole range of therapeutic study of more importance than the manifold therapeutic relations of the nervous system, and none more difficult. The difficulty lies not only in the complexity of the problems, but in the want of exact data for their solution. I shall not attempt to cover the whole ground, but merely to indicate the bearing of a few familiar phenomena, as an introduction to special and more thorough studies hereafter.

In highly-developed organisms, such as any of the lower mammals, the nervous system is of extreme importance, on account of its functions in governing the processes of organic life and in regulating the exercise of the functions of animal life. Man, in addition to these, has the exquisitely-developed nervous mechanism of the mind, whose states react in so intricate a manner upon bodily conditions. In order to facilitate our present studies, it will be necessary to entirely ignore the psychical factor; but even so, we have still

* Delivered in the Philadelphia Polyclinic Evening Lecture Course, February 24, 1891.

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a complex mechanism, with far-reaching and insufficiently understood relations, to deal with.

In the protozoa, the undifferentiated protoplasm possesses not only *irritability*, or the power of response to stimulus, but also the power of originating action, or *automatism*. As we proceed higher in the scale of development, while irritability is retained by all the cells of the body, automatism becomes more and more restricted, until at last it is almost exclusively lodged in the specialized tissue which we call nervous matter. The other cells normally act only in response to stimulus of nervous origin, which thus becomes the governing power. When, however, in the normal exercise of reproductive function, the ovum, a cell devoid of specialization, is produced, it contains within itself all the potentialities which, having been *e*volved, must have been *in*volved in the primordial *zoon*. Most fundamental of these is the nutritive automatism. This fact is of importance in studying the processes of inflammation, repair, and neoplasm-building.

The simplest nervous mechanism consists of three parts,—a nerve-cell or ganglion, which receives impressions from without, and transmutes them into impulses of action; an afferent nerve-fibre, which conveys these external impressions *to* the ganglion, and an efferent nerve-fibre, which transmits, *from* the ganglion, the impulse, which, on arriving at the peripheral organ, results in action. A nerve-cell of this description may, however, be itself under the control of other nerve-cells, which have the power of preventing or inhibiting its action, or of neutralizing the result of that action; and these inhibitory cells may themselves be under like dominion. Thus, for example, we have the well-known phenomena of reflex action of spinal nerve-cells, as exhibited in the knee-jerk, which, however, is capable of being prevented by the exercise of the will through the cerebral motor mechanism. So, too, in functions which are wholly involuntary, similar phenomena are manifested. Take, for example, the nervous mechanism of heat and temperature reaction, which play so important a part in the maintenance of the life of warm-blooded animals, and which, when disordered by disease, give rise to the phenomena of fever. Heat is produced in the body as the result of certain of the necessary functions of life; and, also, it is highly probable, for the special purpose of maintaining temperature, by oxidation of a certain (*thermogen* of MacAllister) portion of muscular substance. Some of this heat is, through the agency of the nervous system, converted into work, and has no effect upon the temperature of the body. Some is dissipated by radiation from the skin, and in the secretions and excretions, especially in the expired air. When neither converted into work nor dissipated, however, the heat necessarily raises the body temperature, and this temperature would thus be subject to enormous variations on account of the varying demands of the different organs for work and of the varying nature of the voluntary activities, were it not for a special mechanism which regulates temperature. This regulation is accomplished in two ways,—by diminishing the production of heat and by increasing heat dissipation. The regulatory mechanism may, therefore, be looked upon as bearing the same relation to the lower nervous mechanisms, which preside over heat-production or heat-loss, as the brain to the spinal cord. Using the word centre in a broad sense, we then have a *thermogenetic* or heat-producing centre, which stimulates all those processes producing heat, and especially the oxidation of thermogen; a *thermolytic* or heat-dissipating centre, which stimulates respiration, the vaso-dilators, and other mechanisms of heat loss; and a *thermotaxic* or heat-regulating centre, which preserves a proper *balance* between these two. The functions of the thermotaxic centre are probably inhibitory in large degree.

Fever heat being one of the most ordinary manifestations of all forms of disease, it is important that its relations with the nervous system be understood, as far as ascertained facts will permit, so that we can correctly apply therapeutic measures to its treatment.

Hughlings Jackson has shown that the order of dissolution in any nervous mechanism is inverse to the order of evolution. In other words, that which is of latest organization yields first; the pyramid topples at its apex before the base is shaken. The latest organized of the nervous mechanisms of heat is evidently the taxic mechanism. This, as Hale White more especially insists upon, is seen not only by observing its entire absence in cold-blooded animals, its less perfect development in the lower forms of mammals, but also by observations upon infants, whose temperature, it is well known, is subject to great variations from external causes, from internal vegetative processes, and from the emotions. For this reason, too, high temperature in an infant or a child is of less

pathological importance than in an adult. Whether heat-production be increased or diminished, in the normal state of affairs temperature is not apt to vary, save within certain well-defined limits, for the reason that the thermotaxic mechanism causes heat-loss to vary in a complementary manner. When, however, the poison of scarlatina, for example, circulating in the blood, comes in contact with the nerve-cells composing the thermotaxic centre, it interferes with their proper performance of function, and the relation between heat-production and heat loss is *unbalanced*. Balance of function consitutes health; unbalancing is an evidence of disease.

How far, however, the phenomena of fever heat are salutary, tending to preserve the organism and destroy the poison, and how far they are in themselves deleterious, is as yet an unsettled question. I am of those who regard moderate fever-heat as beneficial, both in the light of clinical experience and upon the broad application of biologic doctrines. Its organization in the race as a part of the reaction against toxic agents, is, to my mind, *a priori*, proof of its usefulness. To this subject we will recur in another connection.

Take, again, the case of the circulation. This is regulated by a very complicated nervous apparatus, central and peripheral, with intercorrelating fibres. Undoubtedly the heart-muscle possesses to a certain extent the power of automatic contraction of unstriped muscular fibre, and this power is greatest perhaps in the auricles. But more important is the nervous mechanism. This consists of a peripheral motor apparatus, which, being stimulated by the presence of blood, causes contraction of the muscles; a central apparatus of motion, which also causes contraction under various appropriate stimuli; and a central and perhaps also peripheral apparatus of nutrition, which controls or inhibits the action of the motor ganglia. Further, the activities of the heart must be correlated in a very intimate manner with the activities of the blood-vessels, with the activities of the lungs, with the activities of the digestive and excretory organs, thus requiring an elaborate apparatus of communication or correlation, all of which is furnished by the nervous system; and so in regard to all other functions or organs. The nervous system excites, restrains, controls, and co-ordinates their action.

Thus it is that disease in one organ or tissue is capable of causing an infinite variety of perturbations in organs at a distance. The further removed it is from the periphery, the greater the number of communicating fibres affected by disorder in the nervous system, and therefore the wider the distribution of secondary disturbances; but disturbance at the periphery may, by so-called reflex disturbance of a centre, simulate central disturbance in degree and area of secondary effects.

While thus the intimate connection and wide distribution of nervous tissues render intricate and confusing the phenomena of disease and of recovery, they also help us, by directing our therapy against some central disturbance, to antagonize a number of morbid phenomena with a single remedy.

The points which we have to consider specially in directing our attention to the therapeutic activities of the nerves are, first, *nutrition;* and, secondly, *special function of tissue innervated*. Most of what I have time to say will be confined to the first of these themes.

The body being a congeries of cells, grouped into organs, each cell having, in addition to sustentation of its own life, a certain function to discharge in the economy of the whole, the nutrition of the body depends first upon the nutrition of the cells; while the nutrition of each cell depends upon its being furnished with proper materials therefor through the functional activity of some other cell. Therefore, not only must the nutrition of each cell be provided for, but it must be kept functionally active, in order that it may do its share towards the nourishment of the others. In truth, nutrition ought to be a broad enough term to include not only assimilation (upbuilding of tissue, or *anabolism*), but also the *dis*assimilation (breaking-down of tissue, or *catabolism*, with expulsion of *débris*, or *excretion*), which is a necessary concomitant of the exercise of function. We may, therefore, consider either that every cell is supplied through the nervous system with two sets of impulses, —anabolic or nutritive and catabolic or functional;—or that the anabolic phase of nutritive power remains with it as an inheritance from the primordial automatism, while the catabolic phase, being coextensive with function, has passed under nervous control. I know of no experiments which are conclusive as to this point. From clinical observation, I should say that in all probability the potentiality of anabolic automatism remains with cells, but that when normal relations prevail, the process is actually under nervous control.

The health of the body as a whole depends

upon the proper *quantitative* performance of both sets of activities. But the health of the cell itself depends upon maintenance of the proper rhythm between them, which, in this sense, may be called *qualitative* performance. Undue preponderance of either means disturbance, and disturbance in one part is necessarily the cause of disturbance, greater or less, in all other parts.

The first point to be determined, then, whether in relation to disorder of the whole system or to disease of a particular part, is in which direction the balance of function has been disturbed; whether there is undue preponderance of cell nutrition, building up the individual at the expense of the society, or whether there is undue preponderance of functional activity, breaking down the individual, and in this case, as in all others, with loss rather than gain to the society.

In most acute febrile disorders we find the latter to be the case; in most inflammatory conditions, the former is the case, with certain modifications to be pointed out; and in a great many cases the phenomena are so involved that, in the present state of knowledge, we cannot pronounce positively. One process may predominate in one part of the organism, the other, in other parts; as, for example, in tumors associated with cachexia and wasting, or in inflammations associated with fever.

We have already seen that in fever the thermotaxic mechanism is in disorder, in most instances probably as the result of a toxic agent circulating in the blood. The control, inhibition, or *anabolic* function is thus diminished; and the thermogenetic mechanism, being unrestrained, produces increased oxidation of thermogen,—that is, *hypercatabolism*. The result is the wasting of tissues, so commonly observed. The tendency to the production of bed-sores upon very slight mechanical pressure is another evidence of this condition.

Graves appreciated these facts from a clinical stand-point, when "he fed fevers;" though there are other circumstances, too, governing the feeding of fevers, beyond the scope of our present study.

What indication for treatment can we derive from this method of viewing pyrexia? First, we must consider more attentively a matter briefly alluded to a short time ago. It is important that disease and recovery should be looked upon as parts of one continuous process.

The distinguishing characteristic of living things is their ability so to adjust themselves to changes in their environment, or so to adjust some of their parts to changes in other parts, that the general equilibrium may be maintained. This process of adjustment is continuous in every living thing. Just as the balanced action of centripetal and centrifugal forces serves to keep the planets in their orbits, so the balanced action of destructive and constructive forces serves to maintain the even tenor of life and health. Let either predominate, and we have that disturbance, that *unbalanced condition*, called disease; for hypertrophy (overgrowth,—*i.e.*, *excess of construction, hyperanabolism*) is as much a disease as hypotrophy (want of growth) or atrophy (wasting,—*i.e.*, *excess of destruction, hypercatabolism*).

But the inherent tendency of life, confirmed and organized throughout all the ages of evolution, is to restore the disturbed balance of forces. So soon, then, as, from whatever cause, the *balance of function* we call health is disturbed, and the *unbalanced condition* we call disease is originated, the *inherent tendency to restoration* (*vis medicatrix naturæ*) is called into action, *compensatory disturbance* is set up, and its phenomena become commingled with the phenomena of disease.

To learn to separate in his observation the disturbances of disease from the disturbances of recovery is the most important, as it is the most difficult, task of the student of the art of healing. Its accomplishment in many cases is impossible for want of exact knowledge. Still, we may do much towards improving our knowledge by a careful study of the part taken by the nervous system in the production of these phenomena.

It is a doctrine at least as old as Hippocrates that fever is a conservative process. In its most modern form this doctrine represents the high temperature as destructive to micro-organisms. It is also a well-known fact that heat affects the action of certain drugs, and various experiments have recently been undertaken to show that a moderate fever-heat lessens the toxic effects of the chemical poisons produced in the body by pathogenic microbes; but the evidence is, as yet, too uncertain to lay much stress upon.

Much, however, seems to be beyond reasonable doubt.

Heat applied externally is one of the most valuable therapeutic agents in bringing about resolution of non-suppurative localized inflammation, as cellulitis of an extremity, peritonitis, pleuritis, and pneumonitis at certain stages.

Heat externally, and by means of hot

drinks, to promote diaphoresis and "bring out the eruption," is often resorted to in sluggish cases of measles and other exanthemata, and, upon success of the measure, alarming symptoms disappear.

Heat externally and hot drinks had often to be applied by me in the recent epidemic of influenza, because of a coldness and want of circulation, associated with a tendency to collapse; and prolonged subnormal temperature was a marked feature in this class of cases. In one case it was the only objective sign of disease detected.

In cases of threatened collapse in various affections with which we have had experience, and in cholera, with which I fortunately have had no personal experience, we all know or have read of the great value of heat.

On the other hand, experiments have conclusively shown that greater temperatures than any commonly met with in fevers can be borne by animals for long periods, and that many of the evil results attributed to this heat by former observers cannot be confirmed. Clinical experience, too, multiplies the number of patients known to recover from high temperatures and the number of deaths attributed to the depressing effects of heroic doses of antipyretic drugs. These two lines of observation are further coincident with what might reasonably be deduced from the doctrine of natural selection; that the organization of pyrexial tendencies in the race is an evidence of their protective power.

We need, therefore, not hesitate to affirm, even upon this incomplete presentation of evidence, that the pyrexia of fever is, when within limits, an evidence of the tendency to recovery, and is not to be too hastily interfered with.*

The reaction of the organism against the attacks of disease is not always confined, however, within the limits necessary to restore equilibrium. If it were, the physician, like Othello, would find his "occupation gone." Whether from greater instability of organization in certain persons, so that dissolutional processes cannot be brought again under control by the inherent forces of the organism, or from whatever reason, we do at times find symptoms indicative of dangers arising from *hyper*pyrexia. I do not think, however, that we can define the limit between salutary pyrexia and dangerous hyperpyrexia by a line on the thermometer. We must be guided by the association of symptoms, and it is very possible that some of these untoward symptoms may be due to the poison of the disease and not to the heat.

They are those, in general, of profound nervous disturbance,—feebleness and irregularity of the action of the heart, dyspnœa and irregular respiration, insomnia or somnolence, delirium or coma vigil, arrest of secretions, and the like.

They indicate loss of control by higher centres, unrestrained, inco-ordinate action of lower centres and of peripheral mechanisms,—complicated as well by loss of functions in parts unsupplied, or supplied imperfectly or perversely, with blood or with the materials upon which to perform function.

These symptoms demand therapeutic intervention, and it is a fact that, in typhoid fever, for example, where they are often most marked, they may be made to disappear by a measure which also reduces temperature; but—and this is the important point of practice—that measure is not one which directly depresses the nervous apparatus of heat production.

We have seen that high temperature is not an index of increased heat production simply, but of an increase of heat production *relatively* to heat loss. This is an evidence that the thermotaxic centre has been overthrown, or that the ordinary thermotaxic mechanism is inadequate. We, therefore, turn our attention directly to the lower centres. We can reduce temperature by depressing the thermogenetic centre or mechanism, or by stimulating the thermolytic centre or mechanism, or by artificial thermolysis,—namely, abstraction of heat,—the ends aimed at in the two former methods being accomplished by the use of drugs, the latter being carried out by cold bathing, sponging, ice packing, and the like.

We have drugs, such as antipyrin and its congeners, which exercise a powerful effect in reducing temperature, by depressing thermogenesis. If, however, we study closely the effects of these drugs, we find that not only is the reduction of temperature transient, but that it is often accompanied by depression of

* In an "analysis of one thousand cases of acute lobar pneumonia treated at the London Hospital between the years 1880 and 1890," Fenwick (*Brit. Med. Journ.*, January 31, 1891) found that those cases presenting an average temperature of about 103° F. were attended with *the minimum of mortality*, "the states of hyperpyrexia and apyrexia corresponding to the maximum of danger to life." It appears, further, that thirty-five per cent. of all the deaths coincided in time with the sudden defervescence in temperature, the only period more fatal than this being that of the height of the fever. In other words, it is extremes only that are to be dreaded.

other functions which are necessary to the preservation of life,—cardiac and respiratory action, disassimilation, tissue respiration, secretion, and excretion. The action of the poison, then, is not confined to the heat-producing centre, but affects nervous centres of organic life in general; and it is, therefore, to be avoided, as a means of reducing temperature simply, save in extreme cases and with great caution, for temporary purposes. We have as yet no safe drug with which to depress thermogenesis without the risk of affecting other functions injuriously. This method must, therefore, be set aside.*

Thermolysis may be stimulated by opium in appropriate doses (when this drug is not otherwise counterindicated), nitrous ether, the saline diureto-diaphoretics, and other agents acting upon the lungs, kidneys, skin, and vessels. The amount of reduction of temperature which can be thus effected is not marked, and in all but mild cases such measures have only auxiliary utility.

The method of artificial thermolysis, or abstraction of heat by cold sponging, cold bathing, etc., has in its favor clinical experience, and on theoretical grounds can be best defended. It is very probable, too, that the cold acts upon thermogenesis peripherally,—that is, it checks the oxidation of muscular substance without reference to the nervous impulses, and thus opposes hypercatabolism without depressing general vital functions. It acts also reflexly to allay the central nervous disturbance, and thus tends to restrain abnormal central action without undue depression of normal function as well. In brief, the thermotaxic centre having been deranged and unable to co-ordinate heat-loss with heat-production, the therapeutist steps in to supply the deficiency. He increases the dissipation of heat, with as little disturbance of other functions as possible, and without interfering with that normal reaction of the organism which is so potent a factor in recovery.

In inflammations, we have said, the processes of anabolism are unduly increased. So far as the cells participating in the inflammation are concerned this is undoubtedly true; it is not true as to the organs, for these suffer in nutrition just in proportion as the nutrition of the cells is unduly increased. It is a condition of dissolution of society, the individual flourishing at the expense of the whole. Further, as organs are made up of various tissues, the higher and more specialized tissues are crowded out and destroyed by the abnormal growth of the lower and less specialized tissues; just as in revolution and riot—even justifiable revolution—the higher orders of citizens suffer the most. Thus, with undue preponderance of cell nutrition, cell function is lost, and the whole organism, therefore, suffers a deprivation of nutritive materials.

How is the abnormal cell nutrition of inflammation manifested? By reproduction. Inflammation produces a reversion of organized structures to aggregations of undifferentiated embryonic cells. As the process continues, the new cells may finally be deprived of nutrition by mechanically cutting off their own blood-supply, and in other ways; and may thus perish, be absorbed, and resolution occur. This is the normal restoration of balance of function. Or they may fall victims to pyogenic organisms, and suppuration take place. This may aid recovery or introduce new dangers, according to the location of the abscess and other points we cannot now consider. It is also to be noted that the *new cells* of (morbid) inflammatory tissue are no longer under nervous control; they are automatic in their nutrition and incoordinate in their activity; and, although derived from the organism containing and sustaining them, are in reality parasites. They are rioters, who, having become anarchists, are public enemies. But the essential characteristic, from our present point of view, is the abnormal nutrition of individual cells. All other phenomena are secondary to this.

The phenomena of inflammation, then, *in so far as they pass the limits of normal reaction*, have occurred in response to an abnormal impulse, which, whatever may be its detailed mechanism, is, in relation to the cells stimulated or let loose from control, of an anabolic nature. If, now, the therapeutist can divert or neutralize the nervous impulse of supernutrition, reproduction does not take place,

* Quinine and salicylic acid, with their congeners, often reduce temperature safely, but more probably by destroying the disease poison, as specifics in certain diseases, and we must, therefore, exclude them from present consideration. In massive doses and in general cases, as antipyretics simply, they, too, are to be avoided. Phenacetin, acetanilide, and others of the newer drugs are not so dangerous as antipyrin, and all have their legitimate uses; but we are here dealing with broad principles only, not specific details. The dangers attending their use should never be forgotten, as we never forget the dangers attending the use of opium and arsenic. But there seems to be a tendency to use these new poisons of the laboratory empirically, with insufficient indication and without adequate caution.

and inflammatory tissue is not formed. Here we have a possible explanation of a part of the action of opium in controlling inflammations. Opium intercepts the diseased impulse, whether upon its way to the centre or in its transmutation at the centre, and thus averts the abnormal stimulation of, or the abnormal loss of control over, the anabolic processes. In all probability the reason why codeine has a special advantage over all other of the derivatives of opium in this application is because it most possesses this power. As yet we do not know why it is that drugs should act in this manner or in the other, but if it should be found, as Brunton has suggested, and as seems plausible, that the phenomena of pharmacology are phenomena of wave interference, we should explain this action of codeine by the size or rate of its wave movement.

To show another application of the doctrine here presented for your reflection, let us take an illustration in which we have a deficiency of anabolic impulse, the so-called condition of neurasthenia. These cases are characterized by the absence of definite organic disease, yet there is wasting of tissue and inability for exertion, a vicious circle acting and reacting to keep up both phases of the disorder. Feeding, improving digestion merely, will not suffice. We administer strychnine, a catabolic agent, whose power is, by stimulating organic processes, to promote the breaking down of tissue. We administer oxygen, the great consumer, the *Loge* of science, and arsenic, an agent which probably destroys tissue; and yet, although we have given agents, the action of which is to increase the breaking down of tissue, the net result is that the patient increases in nutrition. The reason is obvious. Health depends upon a proper balance between cell-nutrition and cell-function. The impulse of nutrition is called forth by the exercise of function, and function is again rendered possible by the rebuilding effected. But, unless function goes on, nutrition cannot take place. Living tissues are not like inanimate matter, capable of indefinite continuance in quiescence. Life is normal life only when both its phases rhythmically alternate. In neurasthenia this is not the case. Its starting-point may have been indigestion, lessening nerve-nutrition; or too great nervous exertion, leading to exhaustion; or a combination of causes may have been at work. Impaired nutrition lessens capacity for function. Lessened function reduces nutrition. There is a vicious circle, and we must choose some one point at which to break it. When, by our therapeutic measures, we have restored the functional activities of the cells, we have restored that condition of the cells which sends to the equilibriating or taxic centre the needed impulse of upbuilding, and in response to that restored normal stimulus we have a restoration of proper nutritive activity.

These are but a few sketchy and imperfect illustrations of the influence of the nervous system in and over disease and recovery.

The subject cannot be thoroughly elucidated in anything short of an elaborate treatise. But the little we have seen may induce us to pay more conscious attention to this phase of the therapeutic science, and, as physiology and pathology give us increased and more exact information, to seize upon that information, and use it in the service of the art of healing.

HEAT PHENOMENA IN CURARIZED ANIMALS.

By Edward T. Reichert, M.D.,* Philadelphia, Pa.

Part I.

THE extraordinary ability of curare to abolish completely the movements of the voluntary muscles without, as a rule, seriously affecting the other important functions renders it of inestimable value in the study of phenomena which demand absolute muscular quiet; and, next to anæsthetics and analgesics, there is perhaps no agent more valuable in the laboratory. Notwithstanding its recognized value and almost universal employment by vivisectors, our knowledge of most of its important physiological actions is largely of a very general nature and far from being satisfactory.

A somewhat extensive series of researches on the heat mechanism in animals, which has been in progress for some years in our laboratories, has necessitated the employment of curare. The absence of sufficient knowledge of the actions of this substance on the heat functions has demanded its study. Since in this work it only has been necessary to use quantities just sufficient to abolish voluntary motion, the experiments have not extended beyond the employment of small doses. Indeed, further than this has not been needful, because the actions of large

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doses are sufficiently understood. The results of this investigation have been of exceptional physiological interest, and in some respects surprising; and while they were intended to serve solely as a basis of certain of our experiments, they are of such immediate value to those engaged in the study of the heat mechanism, or of the actions of various agents upon it, that it has been thought advisable to put them on record in advance even of the fundamental part of the research.

The large amount of heat evolved from muscles as a result of their activity naturally leads to the inference that when these organs are apparently completely paralyzed, as in curarized animals, the formation of heat in them would to a great extent cease, and, as a natural result, there would be a tendency to a diminution of bodily temperature. Coupled with this we have the fact that even small doses of curare dilate the cutaneous capillaries, and thus indirectly increase heat dissipation, thus lowering temperature. The prevalent belief that curare always lowers bodily temperature, therefore, seems based on good theoretical grounds, and there are experimental records which are corroborative. The latter, however, are far from being entirely satisfactory, owing to their limited number, the brief periods of observation, the conflicting results, and the absence of sufficient investigation in the matter of dosage.

Claude Bernard, in observations on rabbits, sometimes noticed a rise of temperature, at others a fall; the rise he attributed to an increased excitability of the sensory nerves. Tscheschichin (*Du-Bois Reymond's Archiv f. Physiologie*, 1866, s. 151), in rabbits of medium size, after doses of ½ centimetre of a two per cent. solution of curare, observed a diminution of temperature of from .10° to 1° C., which progressed gradually to the onset of convulsions, when it rose to a slight extent (.1°), or continued to sink. The rise he thought was due to an increase in heat production in the muscles, and not to the convulsive movements. Fleischer (*Pflüger's Archiv für Physiologie*, 1869, ii. s. 441), in seven experiments on rabbits and dogs, with lethal and non-lethal doses, always noted a primary rise, which was followed by a decrease to the normal, or even below it. He is of the opinion that convulsive movements have nothing to do with the increase. The main features of these experiments are condensed in the above table:

Number of experiment.	Dose.	Animal.	Time after injection of maximum rise.	Amount of rise.	Death.
1	.005	Rabbit.	16 minutes.	1.4°	In 36 minutes.
2	.002	Rabbit.	16 minutes.	0.9°	Non-fatal.
3	.002	Rabbit.	14 minutes.	0.8°	Non-fatal.
4	.001	Rabbit.	16 minutes.	0.2°	Non-fatal.
5	.003	Rabbit.	18 minutes.	0.2°	Non-fatal.
6	.00075	Rabbit.	21 minutes.	0.6°	Non-fatal.
7	.00125	Dog.	4 minutes.	0.4°	In 33 minutes.

In Experiments 6 and 7 curarine sulphate was used.

Hogyes (*Archiv für Exp. Path. u. Phar.*, xiv. s. 138) found in one of two experiments on rabbits, after injecting .001 gramme under the skin, a fall of 1.32° C.; and in the other, after a dose of .002 gramme, a preliminary rise of .44° C., which was followed by a fall. Death occurred in the first in one hour and thirty minutes, and in the second in twenty-six minutes. Riegel (*Centralblatt f. Med. Wiss.*, 1871, s. 403) noted a fall which he believed was due to diminished metabolism. Claus (*Hoffmann and Schwalbe's Jahresberichte*, Bd. i., 1872, s. 599) also records a diminution. Falck (*Pflüger's Archiv für Physiologie*, Bd. xxv. s. 565) states that in four experiments out of five on dogs, in which sublethal doses were used, a primary rise occurred. The following tabular statement is of interest:

Number of experiment.	Time of death.	Temperature. Difference between			Time of occurrence of highest temperature.
		Beginning and end.	Highest and lowest.	Beginning and highest.	
1	15 minutes.	—0.6°	0.8°	+0.2°	7 minutes.
2	19 minutes.	—1.1°	1.4°	+0.3°	7 minutes.
3	25 minutes.	—1.0°	1.3°	±0.0°	0 minutes.
4	28 minutes.	—1.5°	1.6°	+0.1°	15 minutes.
5	29 minutes.	—1.0°	1.1°	+0.1°	4 minutes.

Mosso (*Virchow's Archiv*, Bd. 106, s. 80) also has noted an early increase. Voisin and Liouville (*Centralblatt f. Med. Wiss.*, 1867, s. 414) state that the therapeutic employment of curare in man caused fever, the axillary temperature being increased from 1° to 2° C., the febrile condition lasting for many hours, and gradually diminishing. Kemp (THERAPEUTIC GAZETTE, March 15, 1889), in some careful studies, by far the most valuable on record, obtained results which varied with the dose. He found that small doses caused an immediate rise in rectal temperature, the extent and duration of which depended upon the dose and temperature of the surroundings. Large doses caused a transient rise, followed by a steady fall, the rapidity of which was owing somewhat to the dose, but especially to the temperature of the surroundings. A rise of temperature always occurred, he states, and in some of his experiments remained hypernormal for hours, and even after the recovery of voluntary motion. The doses which he employed varied from .24 to 4.55 milligrammes to the pound of body-weight, and were usually given by the vein. He, moreover, is the only one who has attempted to study by the direct method the actions on the processes of heat production and heat dissipation. These results will shortly be referred to.

While the conflicting statements of these investigators are explained in part by differences in dosage, variations in the temperature of the surroundings, the uncertain composition of the curare, and other less important circumstances, it seems as though there was much not as yet understood.

For reasons already stated I was led first to make a number of experiments on the actions on the bodily temperature, and finally to ascertain more definitely the alterations which are caused in the heat mechanism. This research, therefore, comprises two classes of experiments,—one on the changes in bodily temperature, and the other on the alterations in the processes concerned in heat production and heat dissipation. In all of these dogs were used. The curare was from an original package, as put up by the Indians of South America, and was presented to me by Dr. S. Weir Mitchell, who obtained it through the Smithsonian Institution.

FIRST SERIES.—*The Effects on Temperature.*—In this series the dogs were tied in the conventional trough, lightly etherized, a tracheal tube inserted, the external jugular vein exposed, and the effects of the anæsthetic allowed to pass off. A thermometer was then inserted into the rectum, and, after the mercury had ceased to rise, a record was made, and a quantity of a two per cent. filtered solution of curare was injected into the external jugular vein drop by drop at intervals of a few seconds until the characteristic influences on the muscles became apparent. Artificial respiration was then begun and maintained, and in the course of a few moments complete paralysis of voluntary motion supervened. The quantity of the solution ordinarily required varied from ½ to 1 cubic centimetre, this being sufficient to maintain complete muscular quiet for an hour to an hour and a half, or longer. As soon as the appearance of twitchings indicated the return of voluntary motion, a small quantity was again injected, and this repeated as often as necessary. In several experiments, however, the doses were given more frequently, and in much larger quantities, than absolutely required to arrest voluntary motion, but in these instances with special objects in view, as will be made apparent.

After the thermometer was once inserted it was kept continually in place during the entire periods of observation, which lasted from three-quarters of an hour to seven hours, records being made generally at intervals of fifteen minutes. Nineteen experiments were thus performed on normal animals, the records of which will be found condensed in the table given below.

A study of these records will elicit many interesting facts, but a want of space will prevent more than a general examination. It is at once noticeable that a preliminary rise of temperature has not invariably occurred, as was found by Kemp. In only seven out of nineteen experiments did the temperature at any time go above the normal standard, and in the other twelve a more or less marked diminution was noted.

In Experiment 1 the temperature fell .55° during the first hour and a half, and then showed a slight tendency upward. A second injection had no immediate effect, but at the termination of the next hour there was a gain of .2°, and the temperature continued rising notwithstanding repeated injections. The normal was regained at the end of four and a half hours, and at the end of six and a quarter hours the temperature was .6° in excess. In Experiment 2 there was a decrease of .5 during the first fifteen minutes. This was followed by a slight rise, the temperature remaining at about the same point above normal

Time.	Exp. 1.	Exp. 2.	Exp. 3.	Exp. 4.	Exp. 5.	Exp. 6.	Exp. 7.	Exp. 8.	Exp. 9.	Exp. 10.	Exp. 11.	Exp. 12.	Exp. 13.	Exp. 14.	Exp. 15.	Exp. 16.	Exp. 17.	Exp. 18.	Exp. 19.
hrs. min.	14 kilos.	14 kilos.	24 kilos.	26 kilos.	12 kilos.	7 kilos.	27 kilos.	17 kilos.	6.5 kilos.	5 kilos.	5.5 kilos.	5.3 kilos.	14 kilos.	24 kilos.	9 kilos.	22.5 kilos.	12 kilos.	27 kilos.	11 kilos.
.00	39.15	40.55	40.90	38.50	38.55	39.00	40.30	39.80	39.20	39.05	38.90	39.40	39.00	39.00	39.55	38.60	39.00	39.55	38.70
.15	38.90	.50	41.00	.75	.53	.—	.25*	.55	38.80	38.90	.45	38.85	38.95	38.85	.50	.30	38.35	.42	.70
.30	.65	.60	.05	.80†	.55	.—	.30	.50	.65*	.88	.20	.40	.75	.72	.42	.12	.00	.44	.50
.45	.68	.60	.05	.83	.55	.—	.42	.50	.51	.85	.18	.32	.63	.70	.41	.09	.87	.46	.22
1.00	.70	.65	.10*	.87	.56	.10	.52	.40	.37	.88	.10	.25	.55	.62	.43	37.70	37.70	.45	.10
.15	.70	.70	.10	.95	.55*	.—	.50	.35	.25	.78	37.85	.15	.45	.60	.44	.55*	.37	.37*	37.92
.30	.60	.72	.10	39.07	.55	.17	.53	.40	.15	.60	.80*	.15*	.15	.65	.45*	.60	.22	.37	.75
.45	.65	.67	.20	.25†	.80	.—	.55*	.45	.05	.55	.80	.25	.15	.62	.37	.55	.15	.32	.70
2.00	.65*	.72	.30	.35	.85	.24	.55	.40	37.95*	.60	.80	.35	.20	.65	.37*	.40	.00	.27	.73
.15	.65	.72	.40	.65†	.90	.30*	.57†	.32	.85	.70	.92	.40	.25	.75	.32	.40*	36.95*	.20	.72
.30	.85	.72*	.42*	.90†	.83	.—	.50†	.30	.80	.57	38.10	.50	.35	.75*	.32*	.45*	37.02	.15	.76
.45	.90	.75	.50	40.17†	.80*	38.96	.42†	.20	.75	.60	.15	.50	.40	.70	.27	.47	.02	.10*	.75§
3.00	.95	.90	.50	.45†	.95	.—	.35†	.25	.90	.—	.25	.60	.42*	.72	.20	.57	.10	.05	.45
.15	.80	41.12	.60	.60	.92	.—	.35	.25	.—	.65	.25*	.60	.45	.72	.15	.60*	.22	.00	.75
.30	.87	.30	.80	.96†	.90	.80	.30†	.35*	38.00	.60	.20	.70	.55	.—	.10*	.55	.40*	38.92	.95
.45	.95	.40	.85	41.23‡	.....	.—	.15†	.55	.—	.—	.22	.—	.65	.90*	.05	.55	.55	.90*	.80
4.00	39.00*	.60	42.05	.—	.....	.75	.15	.50	.—	.80	.27	.70*	.75*	.—	.—	.65	.67	.89	.75
.15	38.90	.75	.25	.60‡	.....	.....	39.95†	.40	.—	.....	.50*	.85	.70	.75	39.00	.75*	.75	.85	.55
.30	39.10	.90	.40	.80	.....	.....	.80	.35*	.35	.....	.70	.90	.75	.60	38.92	.80	.95	.85	.55
.45	.30	42.00*	.65	42.05	.....	.....	.80	.35	.—	.....	.—	.—	.60	.58	.90*	.90	.90	.90	.55†
5.00	.28*	.20	.83	.32	.....	.....	.78‡	.30	.—	.....	.70	39.10	.73	.45*	.89	.90*	38.15*	.91*	.70
.15	.20	.45	43.20*	.40‡	.....	.....	.65‡	.30	.—	.....	.—	.—	.78	.32	.85	.90	.15	.99	.70
.30	.50	.52	.62	.60‖	.....	.....	.55‡	.30	.—	.....	.80	.20	.80	.40	.85	.92	.15	39.07	.85
.45	.67	.60	44.05	43.00	.....	.....	.45	.30	.—	.....	.—	.—	.75	.35	.90	38.00	.30	.10	.93†
6.00	.68	.78	.35	.30‖	.....	.....	.45‖	.30	.50	.....	.90	.25	.70	.....	.91*	37.90	.32	.17	.87†
.15	.70	43.20	.35	.25	.....	.....	.50	.25	.....	.....	.50	.—	.75	.....	.99	.90	.47*	.18	.87
.30	.....	.50	.45	.20	.....	.....	.....	.....	.....	.....	.....	.25	.....	.....	39.07	.....	.42*	.20	.87§
.45	.....	.75	.35	.—	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.85
7.00	.....	.80	*d.*	.—	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.83
Gain or loss.	+0.55	+3.25	+3.55	+4.80	+0.35	—0.25	—0.85	—0.60	—1.45	—0.50	—1.10	—1.25	—0.85	—0.68	—0.70	—1.20	—2.05	—0.70	—1.15

* Injected intravenously .007 gramme of curare.
§ Injected intravenously .040 gramme of curare.
† Injected intravenously .014 gramme of curare.
‖ Injected intravenously .060 gramme of curare.
‡ Injected intravenously .020 gramme of curare.
d. Dead.

(.15°) until the end of two and three-quarter hours, when it began to rise steadily and rapidly, reaching at the conclusion of the seventh hour 43.80°, or 3.25° in excess of normal. In Experiment 3 the temperature began to rise immediately, and continued gradually to increase during the entire period of observation of six and three-quarter hours, when a record of 44.35° was obtained, the dog dying within the next fifteen minutes. The gain here was 3.55°. In Experiment 4 a similar result was noted, the temperature beginning at once to increase and continually rising, until at the end of the six and a half hours, when there was a gain of 4.75°. The enormous amount of curare injected in this experiment makes it of unusual interest. In Experiment 5 no appreciable change was noted during the first hour and a half. A second injection was given. The temperature then increased, the maximum being reached at the end of three hours, representing a rise of .4°. In Experiment 6 there was an increase during the first two hours equal to .3°, which was followed by a fall to below the normal. In Experiment 7 there was a decrease of .05° during the first fifteen minutes, then a slight rise occurred, reaching from .2° to .27° in excess of the normal, the maximum being attained at the end of two and a quarter hours. At this time and subsequently repeated injections gradually lowered it, until at the termination of six hours the temperature was .85° below normal. Excessive doses were also used in this experiment.

Of the results of the other fourteen experiments nothing special need be said further than that they all exhibit the same general downward tendency, especially during the first fifteen minutes, some to a greater degree than others; but during the course of several hours they almost invariably show a decided tendency to return to the normal, notwithstanding repeated injections of the poison. This latter characteristic is well marked in Experiments 17, 18, and 19.

In four other experiments, not included in the above, in which the curare was given hypodermically, and in quantities just insufficient to cause loss of voluntary motion, a primary rise occurred in every case; in two this was followed by a diminution to below the normal, and in the other two the temperature continued above normal during the entire period of six hours' observation. In one of the latter the maximum increase was .45°, and in the other 1.20°.

These results show that curare, in doses just sufficient to cause motor paralysis, acts very differently, and may from the first increase the temperature or decrease the temperature, or produce a primary increase and a secondary decrease, or a decrease followed by a rise above the normal. These variable results from essentially the same doses together indicate that the alterations in temperature are effected by several actions of a very different nature. The fact just alluded to, that in all of the four experiments in which extremely small doses were used a rise occurred; that in Kemp's experiments the rise was particularly marked after the smallest doses, and but transient after large amounts; and that excessive quantities in a single dose cause an immediate and profound decrease, at once suggest that the poison acts primarily as a stimulant, and secondarily as a depressant, on the process of heat production. But the extreme uncertainty of the immediate results following the administration of proportionately the same doses, together with the remarkable increase which occurs in some instances after repeated injections of relatively enormous quantities, and the well-marked tendency of the temperature to rise after a time, even while the animal is thoroughly curarized, controverts this ready explanation, and suggests that the actions are of a decidedly complicated nature.

Leaving for a moment a further consideration of these important points, there are several incidents in the records worthy of special remark, as, for instance, the extraordinary rise of temperature in Experiments 2, 3, and 4. The persistent increase of temperature in Experiment 4 during and after the injection of such enormous quantities of curare is most astonishing. Experiment 7 is an instance where tremendous doses exert relatively extremely little effect. A tolerance seems to be established which apparently becomes greater the longer the animal is under the influence of the drug, so that after a while doses may be given with impunity, and frequently repeated, which, at the outset, would have caused a profound condition of collapse, or even immediate death.

In experiments in which a fall of temperature occurs from the first and progresses, the most rapid decline is usually observed during the first half-hour, the subsequent diminution representing a more gradual descent. In those cases where a decided fall occurs during the first fifteen minutes, the temperature very rarely goes above normal, un-

less it be after the lapse of several hours, as in Experiment 1.

It has also been noted, from the results of a large number of experiments in addition to the above, that in one group of dogs in almost every successive experiment there will be an increase in temperature, while in another there will invariably occur a decrease. Thus, upon one occasion, in six out of seven dogs there was an increase, while at another time sixteen animals were curarized before an increase could be obtained. All attempts to find a reason for this have proven futile, the curare being the same, the temperature of the surroundings and various suggested circumstances not affording any satisfactory explanation. Doubtless some peculiar temporary condition of the animals is the reason for these remarkable phenomena, because similar experiences have been noted by different investigators in their studies of other functions in normal animals.

SECOND SERIES.—*The Effects of Pyrexial Agents in Animals lightly curarized.*—The statements made from time to time that certain pyretics are still capable of causing their characteristic effects in curarized animals, together with the occasional contradictions which follow, have prompted the study of several of them, chiefly *strychnine*, *picrotoxine*, *cocaine*, *caffeine*, and *pilocarpine*. The preliminary procedures in these experiments were the same as in the preceding series. Immediately after the abolition of voluntary motion, and an accurate temperature record obtained, one of these drugs was given, usually injected into the external jugular vein, and generally in quantities sufficient to produce decided effects in normal animals.

Eleven experiments were performed with *strychnine*, the doses varying from .0005 to .002 gramme to the kilo of body-weight. In seven the temperature was increased, and in four diminished. In all of the seven, with the exception of Experiments 23 and 24, the temperature began at once to rise after giving the strychnine. In Experiment 23 it fell during the first fifteen minutes .13°, which was followed by a rise during the next interval which exceeded the normal. In Experiment 24 the temperature was lowered during the first half-hour .9°, when a reaction occurred, and a point was reached at the end of two and three-quarter hours 1.2° in excess, death taking place during the next half-hour. In all of these seven experiments, however, the rise, once being established, continued to increase, with occasional oscillations, until the conclusions of the experiments or death approached. The periods covered varied from two to seven hours, and the rule is a distinct and practically steady increase, the extent of which varied to some degree with the length of the experiments. The greatest increase was noted in Experiment 22, in which the rectal temperature reached 43.12° C. just before death, the gain being 3.92°. In Experiment 20 the increase was nearly as much,—3.82°. In the other experiments the maximum gains were 1.20°, 2.58°, 1.20°, 2.62°, and 1.55°, the average for all being 2.41° for an average period of observation of about four hours.

Of four experiments with *picrotoxine*, in three an increase occurred, and in one a diminution. In the former the gains were 2.18°, 2.15°, and 1°; in the latter the loss was 1.15°. The average period of observation was a little less than four hours.

Four experiments were made with *cocaine*, in three of which an increase was noted equal to 1.82°, 3.60°, and 1.40°, respectively, and in one a decrease of 2.10°.

In every one of six experiments with caffeine an increase was recorded, in three of which, however, a primary diminution occurred of .08°, .15°, and .35°, respectively. The gains in these were 4.50°, .65°, .17°, 3.25°, 4.60°, and .40°.

Four experiments with pilocarpine all exhibit an increase, the changes amounting to 1.80°, 1.65°, .60°, and .10°.

It will thus be observed that an increase of temperature occurred in seven of eleven experiments with strychnine, in three of four with picrotoxine, in three of four with cocaine, in all of six with caffeine, in all of four with pilocarpine. Hence in this series the proportional number of experiments in which an increase was noted is much greater than in normal animals, the approximate proportions being, in normal animals, about 1 to 4; with strychnine, 2 to 1; with picrotoxine, 3 to 1; with cocaine, 3 to 1; with caffeine, 6 to 0; and with pilocarpine, 4 to 0. It would thus seem that each of these agents may increase the temperature in animals lightly curarized, yet is by no means certain that the change in any case was due to other than the curare, because the temperature curves are clearly not those which would be obtained in normal animals; the curve of increase by curare represents practically a straight line, the highest point being attained after the lapse of several hours, and showing a definite tendency to continue rising the

STRYCHNINE.—*Experiments* 20 *to* 30, *inclusive.* PICROTOXINE.—*Experiments* 31 *to* 34, *inclusive.*

Time.	Exp. 20.	Exp. 21.	Exp. 22.	Exp. 23.	Exp. 24.	Exp. 25.	Exp. 26.	Exp. 27.	Exp. 28.	Exp. 29.	Exp. 30.	Exp. 31.	Exp. 32.	Exp. 33.	Exp. 34.
hrs. min.	5.44 kilos.	5.5 kilos.	23.1 kilos.	22.1 kilos.	7 kilos.	30 kilos.	16 kilos.	13 6 kilos.	5.9 kilos.	4 kilos.	5.9 kilos.	11.5 kilos.	17.23 kilos.	6.4 kilos.	12.5 kilos.
.00	38.18*	38.65†	39.20†	38.82†	38.35†	39.00‡	38.80‡	40.35§	39.20‡	37.65‡	39.20‡	39.92¶	39.80¶	38.60¶	39.80¶
.15	.36	.67	.40	.75	37.92	.45	.92	.45	.20	.40	.14	.95	.78	.—	.52
.30	.52	.80	.55	.85	.45	40.00	39.15	.—	.14	.15	.15	40.02	.—	37.80	.40
.45	.65	.80	.80*	39.18	.50	.30	.42	.15	.20	.02	.20	.10	.85	.—	.42
1.00	.95	.87	.92	.55	.65	.50	.56	.—	.—	36.90	.20	.30	.—	.75	.45
.15	39.15	.95‖	40.02	.77	.95	.75	.77	.10	.—	.65	.20	.55	40.20	.—	.55
.30	.35	39.03	.15	.95	38.15	41.11	.89	.—	38.00	.—	39.00	.72	.—	.55	.60
.45	.72	.20	.45†	40.15	.—	.53	40.05	.—	.00	.—	.—	.80	.40	.—	.67
2.00	.86	.35	.72	.25**	.95	.62	.30	.—	.—	.—	38.40	.95**	.—	.45	.75
.15	40.05	.50	.85	.60	39.40	.....	.30	.15	37.90	35.30	.05	41.12	.70	.—	.96
.30	.26	.60	41.10	.73	.—	.....	.40	.—	.—	.....	38 00	.35	.—	.55	40.04
.45	.42	.60†	.30	.86	.55	.....	.50	39.55	.72	.....	37.95	.56	41.30**	.—	.16
3.00	.45	.65	.45	.92	.25	.....	.60	.—	.—	.....	.90	.80	.—**	.55	.22
.15	.43	.75	.70**	41.00	*d.*	.....	.70	.30	.60	.....	.72	.97	.70	.85	.43
.30	.35*	.85	.80	.12	.....	.....	.88	.—	.—	.....	.70	42.07	.—	38.00	.45
.45	.15	.80	42.03	.23	.....	.....	.70	.25	.—	.....	.61	.10	.90	*d.*	.80
4.00	.05	.72	.30	.30	.....	.....	.35	.—	.—	.....	.55	.....	.95	.....	*d.*
.15	.36	.55	.40	.40	.....	.....	*d.*	.10	.55‖	.....	.—	.....	.....	.....	.....
.30	41.05	*d.*	.53	.....	.....	.....	.....	*d.*	.....	.....	.—	.....	.....	.....	.....
.45	.10	.....	.65	.....	.....	.....	.....	.....	.....	.....	.—	.....	.....	.....	.....
5.00	.00	.....	.82	.....	.....	.....	.....	.....	.....	.....	.55	.....	.....	.....	.....
.15	.05*	.....	.85‖	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
.30	.12	.....	.90**	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
.45	.26	.....	.85	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
6.00	.35	.....	43.07	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
.15	.52*	.....	.12	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
.30	.90	.....	*d.*	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
.45	42.00	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
7.00	41.88	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Gain or loss.	+ 3.82	+ 1.20	+ 3.92	+ 2.58	+ 1.20	+ 2.62	+ 1.55	— 1.25	— 1.65	— 2.35	— 1.65	+ 2.18	+ 2.15	— 1.15	+ 1.00

* Injected .0005 gramme of strychnine for each kilo of body-weight.
‡ Injected .005 gramme of strychnine for each kilo of body-weight.
‖ Muscular twitchings.
** Injected more curare.
† Injected .001 gramme of strychnine for each kilo of body-weight.
§ Injected .002 gramme of strychnine for each kilo of body-weight.
¶ Injected .002 gramme of picrotoxine for each kilo of body-weight.
d. Dead.

COCAINE.—*Experiments* 35 *to* 38, *inclusive.* CAFFEINE.—*Experiments* 39 *to* 44, *inclusive.* PILOCARPINE.—*Experiments* 45 *to* 48, *inclusive.*

Time.	Exp. 35.	Exp. 36.	Exp. 37.	Exp. 38.	Exp. 39.	Exp. 40.	Exp. 41.	Exp. 42.	Exp. 43.	Exp. 44.	Exp. 45.	Exp. 46.	Exp. 47.	Exp. 48.
hrs. min.	21 kilos.	25.8 kilos.	13.6 kilos.	7 kilos.	19.5 kilos.	9 kilos.	31 kilos.	8.16 kilos.	6.5 kilos.	17 kilos.	10.5 kilos.	14 kilos.	7.5 kilos.	7.25 kilos.
.00	38.03†	39.40‡	38.10†	38.55‡	38.80§	39.15§	38.00‖	38.45§	37.95§	39.55‖	39.95¶	39.40¶	39.05¶	40.85¶
.15	.26	.10	.—	37.90	.72	.05	.00	.70*	.97	.—	.78	.55	.60	.92
.30	.50	.35	38.00	.—	.75	.00	.00	.80	.—	.20	.90	.80	.65	.—
.45	.66	.48	.—	.65	.82	.00*	.10*	.85	38.26*	.—	.95	40.15	.65	.95
1.00	.83	.75	37.80	.—	.82*	.00	.15	.91	.—	.30	41.10	.30	.—	.40
.15	39.15	40.05	.—	.50	.75	.90	.12	.85	.62	.—	.20	.45	.35	.—
.30	.—	.25	.40	.—	.80	.85	.12	.78	.—	.45*	.35	.40	.—	.23
.45	.45*	.50*	.—	.45	.90*	.80	.08	.—	39.05*	.—	.45	.50*	.15	.—
2.00	.—	.87	.10	.—	.92	.....	.03	.65*	.—*	.50	.60	.50	.12	.40
.15	.85	41.00	.—	.45	39.23*	.....	.09	.70	.12	.—	.65	.60	.—	.—
.30	.....	.40	.05	.50	.50	.....	.17	.75	.—	.58‖	.75	.70	38.67	39.95
.45	.....	.55*	.—	.65	.80	.....	.12	.65	.22	.—	.85	.75	.35	.95
3.00	.....	.72	.10	.85	40.12	.....	.....	.60	.—	.56	.90	.75	*d.*	.....
.15	.....	.90	.—	38.15	.55	.....	.....	.60§	.40	.—	.—	.75*	.....	.....
.30	.....	42.05	.10	.—	41.00	.....	.....	.70*	.60	.60	41.15	.70*	.....	.....
.45	.....	.30	.—	.45*	.35	.....	.....	.85	.70*	.62*	.15	.72	.....	.....
4.00	.....	.52	36.90	.—	.75	.....	.....	.—	40.00	.55	.20¶	.67	.....	.....
.15	.....	.83	.—	.90	42.30	.....	.....	39.55	.35	.60*	.30	.75	.....	.....
.30	.....	.90	.35	.—‡	.87	.....	.....	.95	.58	.65*	.50	.80	.....	.....
.45	.....	43.00	.—	39.35	43.35	.....	.....	40.37	.80*	.82*	.75	.80	.....	.....
5.00	.....	.....	.00	.—	.37	.....	.....	.80	41.00	.95	.60	.80	.....	.....
.15	.....	.....	.....	.45	.30*d.*	.....	.....	41.30	.35	.70	*d.*	.95	.....	.....
.30	.....	.....	.....	.—	.....	.....	.....	.65*d.*	.73	.....	.....	.93	.....	.....
.45	.....	.....	.....	.10	.....	.....	.....	.70	.83	.....	.....	41.05	.....	.....
6.00	.....	.....	.....	.—	.....	.....	.....	.....	42.35	.....	.....	39.90	.....	.....
.15	.....	.....	.....	.40	.....	.....	.....	.....	.35	.....	.....	.....	.....	.....
.30	.....	.....	.....	.—	.....	.....	.....	.....	.65	.....	.....	.....	.....	.....
.45	.....	.....	.....	.65	.....	.....	.....	.....	.65	.....	.....	.....	.....	.....
7.00	.....	.....	.....	.—	.....	.....	.....	.....	.55	.....	.....	.....	.....	.....
.15	.....	.....	.....	.95	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Gain or loss.	+ 1.82	+ 3.60	— 2.10	+ 1.40	+ 4.50	+ 0.65	+ 0.17	+ 3.25	+ 4.60	+ 0.40	+ 1.80	+ 1.65	+ 0.60	+ 0.10

* Curare given.

† Injected .01 gramme of cocaine hydrochlorate per kilo of body-weight hypodermically.

‡ Injected .02 gramme of cocaine hydrochlorate per kilo of body-weight hypodermically.

§ Injected .10 gramme of caffeine per kilo of body-weight hypodermically.

‖ Injected .05 gramme of caffeine per kilo of body-weight hypodermically.

¶ Injected .001 gramme of pilocarpine per kilo of body-weight hypodermically. *d.* Dead.

longer the observations were conducted, and, indeed, until pyrexia itself becomes a fatal element; the curves shown by strychnine, cocaine, etc., in normal animals, represents a rapid ascent and a similar decline, the climax commonly being passed during the first or second hour. The differences in the characters of the curves are strikingly evident when we compare those produced by cocaine and caffeine in normal and curarized animals. They are entirely dissimilar, and in the latter are typical curare curves. Whether the increase in these experiments was due to the curare, or whether the usual course of effects by these drugs on the heat processes is modified in the curarized condition, is not certain. The results of the experiments in the fourth series, which will shortly be referred to, seem to render it apparent that the curare is not altogether responsible.

(To be continued.)

ACTION OF OIL ON THE ANIMAL ORGANISM.

By W. C. Caldwell, M.D., Chicago, Ill.*

THE important action of oils is after entering the circulation, so a knowledge of the conditions for absorption is as necessary as an understanding of how it acts. I will first consider the absorption of oils, and then the action of oils in health and disease.

I. ABSORPTION.

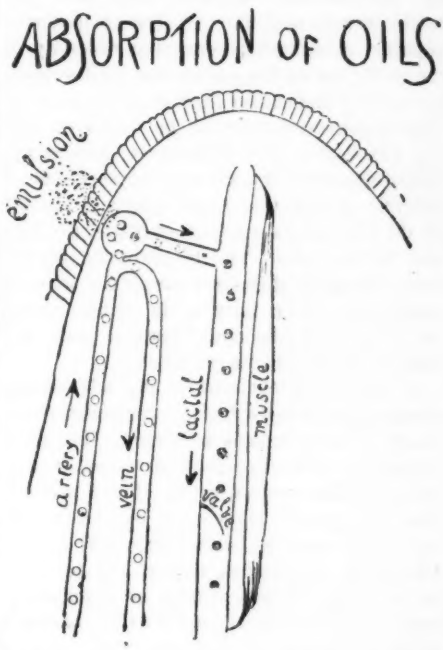
Oils may be absorbed in limited quantity from the skin and mucous membranes by passing into the lymph-spaces, but this is by no means sufficient for the needs of the body in the higher vertebrates; hence the necessity for the differentiation of a special mechanism for the absorption of oils. This mechanism is located in the small intestine. I shall confine myself entirely to a consideration of absorption by this mechanism.

I will present the subject in the following order:

1. Mechanism of absorption.
2. Forces causing the oil to pass inward.
3. Conditions diminishing absorption.
4. Conditions increasing absorption.
5. Relation of liver to absorption of both oils and non-oils.

Mechanism of Absorption.—The millions of villi mainly situated in the duodenum and jejunum constitute the mechanism. As shown in the accompanying diagram (1),

DIAGRAM I.



each villus consists of a conical projection covered by a single layer of columnar epithelium on a basement membrane, beneath which and occupying the villus is a spongy network of adenoid tissue whose intercommunicating channels extend from the lymph-spaces beneath epithelium to a central tube called the lacteal. This lacteal has valves opening centreward, and around it, extending from apex to base, are arranged longitudinally unstriped muscular fibres. There are also some muscular fibres running transversely. As shown in the diagram, a small artery is placed eccentrically in each villus.

1. The route the oil takes in its passage from the intestinal tube to the venous circulation is through the columnar epithelium into the lymph-spaces, and there it enters the white corpuscles, and passes along the irregular lymph-channels to the central lacteal, and then through the chyle vessels into the thoracic duct, which carries it to the subclavian vein.

2. Because the proteids and carbohydrates are rendered capable of osmosis by digestion, they readily pass directly into the portal veins, and hence reach the circulation without taking such a circuitous route.

* Professor of Materia Medica, College of Physicians and Surgeons, Chicago. Abstract of lecture delivered November 4, 189c.

3. But the oils are not so easily handled. Oils have so little affinity for water that they will not osmose, and it is very difficult to convert them into new compounds (unlike the proteids and carbohydrates, which are easily transformed into soluble compounds) capable of osmosis; hence the necessity in the evolution of the vertebrates to develop a special mechanism for their absorption.

4. However, it must not be forgotten that the pancreatic juice attempts to render the oils osmosible, and succeeds to a very limited extent. It does this by splitting a small part of the oil into its component parts, glycerin and fatty acids. The glycerin, having affinity for water, diffuses through the mucous membrane. The fatty acids combine with the alkalies of bile and intestinal juice, and then, as soaps, diffuse inward.

5. But the great part of the oil remains *chemically unchanged*, hence some other means of absorption becomes necessary. The oil is broken up into microscopic particles, each of which is then covered with a film of material that has greater affinity for water than the oil. This coating, having so much greater affinity for the tissues, enables the screened oil to make the trip without so much opposition. The material used for this coating is alkaline albuminate and soap. A mass of these film-covered globules is called an emulsion, and it is mainly by converting the oil into an emulsion that it is absorbed.

6. The bile and pancreatic juice prepare the oils for absorption, and they do this in the following ways:

(1) The bile saponifies any free acid that may be present, so that it can enter the portal vessels.

(2) Pancreatic juice hydrates and splits up a small part of the oil so that the bile may saponify the acid.

(3) Both bile and pancreatic juice emulsify the large remaining portion.

(4) Bile also has another very important function in absorption, and that is, by bathing the mucous membrane the penetration of the oil is greatly facilitated.

Years ago, Wistinghausen showed that oil will rise higher in capillary tubes moistened with bile than in those moistened with water. He also showed that by moistening a membrane with bile the oil will pass through more readily than through a membrane saturated with water. In dogs with biliary fistulæ there is less fat in the chyle and more in the fæces, showing the important relation of the bile.

When in similar ligatured loops of the living intestine oil alone, and oil with bile, are injected, it is found, after the animal is killed, that much more of the oil that was injected with the bile is absorbed.

It is probable that the way the bile increases absorption is due to the fact that the bile has affinity for both water and oils, and hence can take the oil along with it into the water soaked tissue.

Then, in summing up this, remember that the bile promotes absorption—

1. By saponifying the fatty acids.
2. By aiding to emulsify the oil.
3. By moistening the mucous membrane.

Remember also that the pancreatic juice promotes absorption—

1. By hydrating and splitting up the oil into glycerin and fatty acids. The glycerin and the fatty acid as soap, both being soluble, pass into the portal capillaries, and, through the influence of an unknown ferment, unite again to form oil. Perewoznikoff and Will, after injecting soap and glycerin into the intestinal canal, found neutral fat in the villi. Ewald found that fat was formed from soap and glycerin in the presence of the intestinal mucous membrane.
2. By emulsifying the oil.

Having shown that the bile and pancreatic juice—

1. Render a small part osmosible.
2. Render a large part less repulsive by emulsification,

I am now ready to consider what forces—

1. Carry the emulsion through the columnar epithelium, and then—
2. Carry it from there into the chyle-ducts.

It is probable that the epithelium, like the amœba, throws out around the fatty particles pseudopodia, which, retracting, draw the fat into the epithelial cell.

Then, again, it is probable that the affinity of the protoplasm of the epithelial cell for the albuminous film over the oil-globules draws them into the cells.

After having entered the cells they pass through into the white corpuscles in the subjacent lymph-spaces. It is likely that for some unknown reason the corpuscles have greater affinity for these globules, and hence attract them into them.

A part of the white corpuscles in the eccentric artery, as shown in Diagram 1 wander into the lymph-spaces, become loaded with the fatty granules. Then these loaded leu-

cocytes are forced through the lymph-channels into the central lacteal by the pumping force of the villus, brought about by the contraction of longitudinal and transverse muscles pressing the liquid out of the lacteal beyond the valve ; then the relaxation of these muscles, having a tendency to produce a vacuum, draws the leucocytes centreward to be in turn pumped beyond the valve into the chyle-duct.

When you remember the mechanism of absorption you will readily see that absorption will be diminished by diseases which derange—

1. *The liver.*—Any of the acute or chronic diseases which interfere with the secretion of bile just so much disturb absorption of fats. Typhoid fever, where there is extensive degeneration of the hepatic parenchyma, causing light-colored stools, diminishes absorption. When there is a coated tongue, indicating that the liver is not working properly, oils do not agree. Hence, cod-liver oil should be withheld in cases of phthisis and other wasting diseases when the tongue is coated. For this reason, in consumption, where the tongue is habitually coated, not much can be expected from cod-liver oil. People who have small livers are ill adapted for digestion of fats.

2. *The pancreas.*—Any diseases that interfere with the function of the pancreas cripple the emulsification and absorption of the oils.

Of course, to promote absorption of the oils it is necessary to see to the functional activity of the liver and pancreas. *Always clean the tongue before giving oils.* This can be done with calomel and salines.

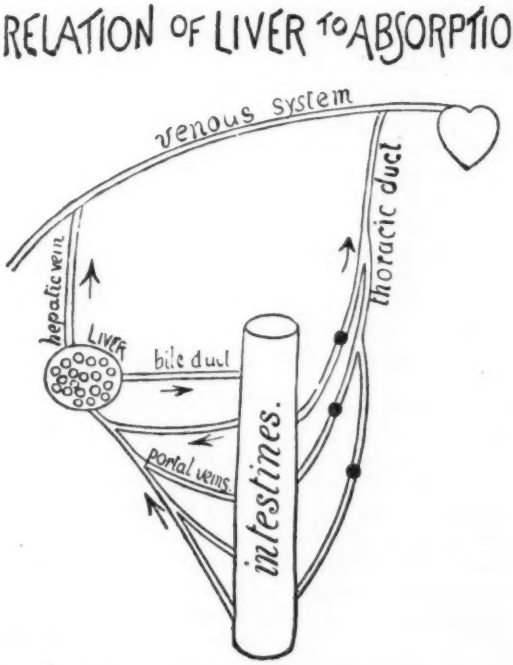
It is said that ether aids absorption by stimulating the pancreas.

In case absorption is still sluggish it may be increased by supplying what nature has failed to do,—bile and pancreatic juice.

From what I have said it is evident that the liver holds an important relation to the absorption of oils, but for an entirely different reason it holds an equally important relation to the absorption of the proteids and carbohydrates.

By examining Diagram 2 this relation will be evident. The oils require a normal action of the liver that there may be a proper quantity of bile to emulsify them so that they can pass to the circulation through the lymphatics. The proteids and carbohydrates do not require a normal liver for that purpose but this relation is due to the anatomical fact that the liver is the gate-way for these materials to pass to the systemic circulation

DIAGRAM 2.



Hence, when this portal is closed their absorption is hindered just as much as the oils are by a deficient quantity of bile.

The practical conclusion to be drawn from this is that, when the liver is out of order all absorption is interfered with, the absorption of all kinds of food is diminished. Hence, when the tongue is coated, absorption is sluggish. Since the absorption of nutrient material is so important to keep up the powers of life, the condition of the tongue should never be overlooked in the treatment of disease.

II. ACTIONS IN HEALTH.

I will consider only the actions of oils after entering the circulation. The protoplasm of a cell consists of its frame-work and the material stored in it that can be used in liberating energy to perform its function, whether glandular, muscular, or nervous. When a muscle contracts, there takes place the combustion of a certain amount of fuel whose liberated energy causes the muscle phenomena. The cell may be compared to a furnace, consisting of the furnace proper and coal. The frame-work of the cell is formed of the proteids and salts, fuel stored in it for combustion consists of fat and glycogen. Hence the oils have a very important function in the cell. Without this fuel, protoplasm would have very little power to work. Every one knows how much more easily oil burns than lean meat. A substance burns easily in proportion to the absence of oxygen from its composition, and the presence of easily oxidizable elements. Fats contain only about ten per cent. of oxygen, the remainder consisting of carbon and hydrogen. For this reason fats possess greater power of force-production than any other alimentary substances. The proteids can be burnt, but it is a very poor fire, and a very expensive fire. For the animal organism to burn proteids (cell-structure) would be like burning the engine-house instead of coal. However, in high fevers this occurs to the great detriment of the patient, resulting in emaciation as the nitrogenous structures are melted down.

The fact that oil is the fuel of the cells produces two distinct effects:

1. It supplies material so that the cells can do more work.

2. This energetic action of the cells increases their vitality. Organs that are inactive atrophy; so with cells, and especially is this marked in the successive generations. If the cells are active, each succeeding generation is stronger; if inactive, each generation is weaker.

The oil, as it were, by increasing the exercise of the cells, develops them. This gymnastic exercise, kept up during successive generations of cells, makes a very marked improvement in the vigor of them.

This secondary action is a very important factor in improving the poorly-developed cells.

There is difference of opinion as to what part of cod liver oil is of such great service.

Wood classifies it as an alterative, and thinks that it has some peculiar action on the blood-making organs.

Bruce regards the action of the oil as a food of the first importance, while the iodine, bromine, etc., are only secondary.

Bartholow thinks that its therapeutic value depends not only upon the oil, but also upon the gaduin and other ingredients.

Chapateau believes that it is the morrhuol that is of service.

The value of an oil is based on the following three facts:

1. Its agreeableness to take.
2. Its rate of absorption.
3. Its rate of oxidation, so that it will the more readily burn and give off energy to the weak cells.

While cod-liver oil is very unpleasant to take, yet it is superior to all others as to rate of absorption and oxidation:

Nauman found, in testing with permanganate of potassium the comparative rate of oxidation of oils, that cod liver oil was much more easily oxidized than the others.

III. SYNERGISTS.

All drugs that by any means improve the vital functions may at some time be synergistic. Hence, those drugs which are foods, as iron, manganese, and phosphorus, are often of great service when combined with cod-liver oil. All drugs that increase digestion, as bitters, acids, etc., by enabling more material for the blood to be prepared, like cod-liver oil, increase the food for the cells. All drugs that increase the functional activity of other mechanisms, as by stimulating respiration purer blood circulates through the tissues, as by stimulating the circulatory mechanism more food is carried to the tissues, are, of course, synergists with cod liver oil in building up the weak cells.

IV. ACTIONS IN DISEASE.

The use of oil is based on the fact that it is the natural fuel for protoplasmic activity

Oil has no specific action in any particular disease, but it simply improves the nutrition of the cell by increasing its power to work. This increased activity improves its power to grow and multiply, and hence there results stronger and more vigorous cells better prepared to battle in the struggle for life. Better able to resist the encroachment of an invading army of pathogenic microbes. The indication for the use of cod-liver oil is where there is defective cellular activity, where there is not sufficient power in the cells to become fully developed and hence die young.

This condition may be inherited or acquired. For this reason cod-liver oil is an efficacious remedy in the scrofulous diathesis, where the cells do not have sufficient inherent vitality to mature, but appear to spend what little energy there is in the excessive proliferation of imperfect cells that soon die. This manifests itself in hyperplasia of the lymphatics, respiratory mucous membrane, and pulmonary alveoli. Since this excessive proliferation of weak cells in the pulmonary alveoli makes a fertile soil for tuberculosis, cod-liver oil, by removing the bronchitis or catarrhal pneumonia, may prevent or even arrest incipient phthisis. It is of equal service where the proliferation is in the ends of the bones, as in chronic arthritis (tuberculosis), or in the shaft of the bone.

But it is not only indicated where this weakness is inherited, but where disease has so depraved the nutrition that the cells do not have sufficient vitality to propagate healthy cells. Hence, cod-liver oil is beneficial at times in the cachexia of tertiary syphilis, in chronic rheumatism, neuralgia, and skin-diseases. It is also of use in the slow convalescence from acute diseases, as from the sequelæ of scarlet fever. Badly-nourished, emaciated infants, suffering with chronic intestinal disorders, are sometimes benefited by inunction with cod-liver oil.

THE CLIMATE OF SOUTHERN CALIFORNIA.

By F. Gundrum, M.D., Escondido Valley, Cal.

I WISH to make a few additional remarks to my article in the November number of the Therapeutic Gazette, and also to note one or two points in a communication from the pen of Dr. C. R. Orcutt, of San Diego, Cal. I was rather indefinite in my remarks as to the diurnal variation of temperature, which I wish to correct by making it more definite.

While living at "Marilon Park," two and a quarter miles from San Diego, I noted a change of 42° F. from 2 P.M. to 6 A.M. the next day, not only once but several times, during January, 1888. During pretty much the whole of the month of November, 1890, we had an east wind,—a strong gale,—during which time the daily variation in temperature was remarkable. The thermometer at my ranch varied, from 2 to 3 P.M. to next morning, from 90°–94° to 38°–44°, the maximum being 94° and the minimum 38° F., making a difference of 56° F. At the lower end of this valley the difference was still greater, amounting to 62° F. During this weather almost everybody contracted cold, all felt badly, and this extended to the lower animals.

Dr. Orcutt makes the statement that "tuberculosis never originates under such climatic conditions as here [San Diego] exist," etc. and "at San Diego tuberculosis is invariably arrested and cured in the earlier stages, and it is only to our equable climate *and the dryness of our atmosphere that this seaport town can claim any peculiar advantages*," etc. (italics mine).

I am very sorry, indeed, that Dr. Orcutt has made such positive and sweeping remarks, as my personal observation is to the contrary. That consumption or tuberculosis never occur in San Diego is a great mistake, and I personally know of at least two cases; and, having been convinced that at least two occurred, he may find others by diligent research.

A young lady died of pulmonary consumption a few years ago at San Diego who lived there from childhood up, dying at the age of twenty-two. It was Miss Cora Nickols, and the doctor can assure himself of the correctness of my statement by interviewing the mother, who lives on the northwest corner of Cedar and Third Streets. I attended a girl, 11 years of age, while I lived in San Diego, who died of tuberculosis of the intestines. This patient was born in the middle of this State, and came to San Diego, in perfect health, three years before her death. There is a lady in this valley (a much healthier place than San Diego) who contracted consumption here, and is now in the third stage of that disease. The doctor is as nearly correct in stating that all cases are cured if they come to San Diego in the earlier stages of phthisis.

The doctor did make one statement which is correct,—viz., that the climate at San Diego

is very equable. There are few places in the world that can boast of a more equable temperature, but when he makes the statement that it is a dry atmosphere, he is away off. It is one of the most humid atmospheres in the world, with this exception, that when the wind from the desert is strong enough to drive back the wind from the ocean, then the humidity is at a minimum. But when this is not the case, the atmospheric humidity runs high. Major-General Stuart Stanly, of the British army, spent two years in this part of the country, and made many scientific observations. He told me that there was only one place in the world where the humidity ranged higher than at San Diego,—viz., at the island of St. Helena. The humidity at San Diego runs all the way from the 70's to the 90's. The statements of General Stanly, and what notice I have taken of the signal service report at San Diego, confirm this.

And last, but not least, I must notice "Poor Lo," the long-living Indian. It is a fact that "Poor Lo" lives a long time here, and so he used to in the South, North, and East. But they do not all live from one hundred to one hundred and fifty years. Some have even died of consumption. The longevity of the native Indian is always open to criticism, as they keep no kind of record of their birth, and a misfortune it is that George Washington did not live out here, so that their age could be estimated to some degree of certainty, like the long-living negroes of the South.

I desire to have nothing but facts put before the medical profession about the climate of Southern California, and the facts are good enough. This valley is probably as fine a climate as can be found in Southern California at the same elevation and distance from the ocean; but there are persons whom I have consulted that cannot live here, but live with great satisfaction ten to fifteen miles farther inland and one thousand feet higher above the ocean-level. Others, who could not remain at San Diego, enjoy life here.

Careful observation, truthfully stated, will set this matter right in the end.

THE THERAPEUTIC USES OF OXALIC ACID.

By A. W. Marsh, M.D., Oriskany Falls, N. Y.

AMONG the many remedies recommended in late years for amenorrhœa, the one that has proved most valuable, in my hands, is oxalic acid, as suggested by Dr. F. Paulet.

It has none of the objectionable, and nearly all of the valuable, qualities possessed by the other emmenagogues. It is not unpalatable, non-irritating to the stomach in medicinal doses, certain in its action, has no oxytocic properties, and, more valuable still, it may be used in all cases of amenorrhœa where an emmenagogue is applicable. I have used it for four years in all such cases with the best effect possible.

It was while using the acid in the above-mentioned cases that I discovered another valuable use of the drug, which I have never seen referred to, and that is its sedative action in acute cystitis.

The following are a few of the many cases in which I have used it, and I have yet to record the first failure.

Case I.—Miss C., aged 26. Had been under homœopathic treatment two or three years for spondylitis and uterine prolapse. Had developed, several months previous to my first visit, a vesical inflammation, primarily from the continued use of cantharidic blisters, without proper precautions. This condition was aggravated and kept up by the prolapsed condition of the uterus. For the cystitis I gave her the following:

℞ Acid. oxalic., gr. xvi;
Syr. aurantii cor., ℥i;
Aquæ pluv., q.s. ℥iv. M.
Sig.—Teaspoonful every four hours.

The result was all that could be desired,—the acute symptoms all subsided immediately, and a few days saw her completely free from the vesical irritation.

Case II.—Mrs. A., widow, aged 75. She has had several attacks of cystitis. Treated her with hyoscyamus, triticum repens, corn-silk, and pichi at different times, with rather unsatisfactory results, the inflammation continuing two or three weeks at a time. When another attack occurred, I gave the above prescription. The result was magical. In less than twenty-four hours the pain, tenesmus, and frequent desire to micturate had all disappeared, and, after two or three days, no evidence of the trouble remained.

Case III.—A. B., aged 18. He retained his urine several hours after a desire to evacuate the bladder occurred. The distention was so great that he had much difficulty in emptying the bladder, when he did make the attempt.

The result was an attack of acute cystitis. The pain and tenesmus were great, and the desire to urinate occurred every fifteen or twenty minutes. Gave the acid, and in two days he was completely cured.

CASE IV.—Mr. W. Had mild attack of cystitis, caused by the influenza. Cured in twelve hours by the acid. In this case the patient doubled the dose, and continued its use for several days after pain and tenesmus of bladder had ceased. From this excess of the acid he had some scalding from urine and griping pain in bowels. This is the only case when such symptoms developed.

CASE V.—Mrs. J., aged 60, married. Complained of frequent desire to urinate, accompanied with pain and straining. Gave the acid, and directed her to avoid straining, etc. Found her better next day. Three weeks later found her worse than ever. The tenesmus was almost constant, and the urine dribbled away most of the time. Her limbs were swollen, and nephritis was suspected, though no albumen was found, but the microscope afterwards revealed casts in abundance. I again gave the acid, and within three days all the pain and straining had disappeared, although some soreness remained several days longer. She was able to retain the urine several hours, and had no further trouble with the bladder.

The above cases have been selected to show the different causes that produced the cystitis in which the acid was used. The cases might be multiplied, all showing the same marked results.

The action of the remedy is rapid and the results certain, and it may be used in all cases of acute cystitis, from whatever cause, care being taken to use either rain- or distilled water, to prevent the formation of oxalate of lime.

THE TREATMENT OF FURUNCULOSIS.

According to DR. VEIEL (*Centralblatt für die Gesammte Therapie*, January, 1891) the treatment of furunculosis includes the observation of the four following indications:

1. The pus-forming micrococci which have penetrated into the skin must be destroyed by antiparasitical measures before they have produced tissue-changes.

2. When tissue necrosis has occurred, the indication is then to accelerate the exfoliation of the dead tissues, so as to remove the micrococci as rapidly as possible.

3. To prevent new formation of furuncles from first infection.

4. To place the organism in such a condition that it may be most capable of resisting the infection of the pus forming micro-organisms.

The author shows that the first of these principles can be accomplished in but few cases if the infection of micro-organisms is so far extended as to lead to visible alterations in the skin and swelling, or to the formation of blisters, for then necrosis has already commenced, and the excretory ducts of the glands are already obstructed by exudation products. Consequently, the introduction of antiseptics into the gland, through friction applied to the external surface, is already impossible. In this condition the use of the carbolate of mercury plaster of Unna, or the concentrated alcohol solutions of boric acid, are of no avail, while the injections of three per cent. of carbolic acid solution, as recommended by Bidder, or the introduction of a silver wire coated with nitrate of silver are both unreliable and extremely painful. Consequently, in the majority of cases, attention must be paid to the second indication above mentioned,—that is, the facilitation of the removal of the necrotic fragment and the microbes included within it. Here the author, contrary to the general modern view, is strongly in favor of warm applications, since he maintains that there is no measure which so rapidly or so certainly leads to the desired result. In order to prevent infection of neighboring parts through the micro-organisms which accumulate on the poultice, he recommends the washing of the skin with a 1 to 1000 sublimate solution or a four per cent. boric acid solution. At night he recommends that the furuncle be covered with an ointment composed of equal parts of oxide of zinc and vaseline with four per cent. boric acid. This ointment is also claimed to fulfil the third indication above mentioned,—that is, to prevent extension of the infection,—while great attention must be paid to cleanliness. The fourth indication is fulfilled by liberal diet; the preparations of iron to combat anæmia and systemic affections must be properly combated. Arsenic he prefers to all other remedies, although he also strongly recommends the use of sulphide of calcium in furunculosis, as well as in impetigo, acne, and sycosis. He condemns the use of cathartics.

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Leading Articles.

RECENT RESEARCHES AS TO THE PRODUCTION OF IMMUNITY FROM DIPHTHERIA.

THE excitement which was evoked by the recent claim as to the prevention and cure of tuberculosis is largely chargeable, if nothing else could be urged against it, with the lack of attention attracted by a number of highly important contributions which have recently been published as to the nature and prevention of diphtheria, and which, to the unbiased observer, afford much more ground for sanguine hope as to the prevention of a scourge scarcely less virulent than tuberculosis; while the unassuming character of the statements made, and the highly scientific nature of the mode of procedure, affords a very pleasant contrast to the tuberculosis furor. With the single exception of tuberculosis, there is no one among the infectious diseases which, in the last few years, has been studied with greater profit. The specific agent of the disease has been recognized, its etiological properties studied, the poison isolated, and its mode of action determined; and while yet much is to be done in determining the exact condition through which immunity to this affection may be conferred, the facts which have been attained are of sufficient importance and value to warrant the greatest hope that ultimate success will soon be attained. Further, the methods of study are not only valuable from the results which have been acquired as regards diphtheria, but especially as to the application of similar methods to the study of the other infectious diseases.

Klebs, at the Congress in Wiesbaden, in 1883, was the first to recognize the presence of the specific bacillus in diphtheritic false membranes and in adjacent mucous membrane, while Loeffler positively stated the existence of the bacillus in twenty-five cases of diphtheria, and was able to obtain pure cultures of bacilli, and to successfully inoculate birds, chickens, rabbits, and guinea-pigs, with the reproduction of the false membrane. Loeffler's results were, however, not accepted without question, for in no case was there any consequent paralysis in cases which did not prove fatal, and similar bacilli were recognized in the mouth of apparently healthy individuals.

Hoffman, in 1888 (*Wiener Med. Woch.*, Nos. 3 and 4), was even more positive than Loeffler as to the specific character of the bacilli, recognizing them located in the false membrane in a large number of cases of diphtheria, while he also stated that they were to be met with in certain cases of scarlatinal angina, and in the sore throat of measles. Such was the state of the question when it was reopened by Roux and Yersin in experiments made in the Pasteur Institute in 1888, 1889, and 1890. In their first publication, these authors stated that they had recognized this specific bacillus in all cases of diphtheria examined, and that they were able to produce not only the false membrane and all the characteristics of a marked case of this infectious disease in the guinea-pig, the rabbit, and the dog, and the fowl, but that diphtheritic paralysis also followed, whether as a consequence of pharyngeal or tracheal inoculation, or intravenous injections, in cases which did not prove fatal. These authors also stated that they were able to recognize the difference between the specific diphtheritic bacillus and the non-violent pseudo-bacillus found in the mouth of healthy persons, or in cases of non-diphtheritic angina. They claimed that this non-virulent bacillus is very rare in fatal diphtheria, is more abundant in the benign

cases of diphtheria, and becomes still more abundant as severe cases of diphtheria progress towards cure, while during the convalescence in such cases it is much more abundant than in the mouth of healthy persons. It would, therefore, seem that there is a close relationship between the two bacilli, the latter apparently being an attenuated form of the former.

These authors' first publications were very shortly followed by papers by Prudden and Northrup, in the *American Journal of the Medical Sciences*, June, 1889, while Babes (*Zeit. f. Hygien*, vol. v. p. 177) found the bacillus of Klebs in forty-two cases of diphtheria.

D'Espine (*Revue Méd. Suis Romande*, 1888, No. 1) found it in fourteen cases of diphtheritic angina, while it was absent in twenty-four cases of non-diphtheritic sore throat. Ortmann (*Berliner Klin. Woch.*, No. 10, 1889) found it fifteen times out of sixteen, while Kalo Paltauf (*Wiener Klin. Woch.*, 1888) found it in fifty cases of diphtheria. Beck (*Zeit. f. Hygien*, Band 8, Heft 3) found likewise the bacillus of Klebs in fifty-two cases which he examined, and he believes that the bacillus appears first in cases of diphtheria, and is then followed by the streptococci, which, penetrating into the circulation, provoke the severe general symptoms characteristic of malignant cases of this disease. No evidence whatever is apparently attainable which will support this hypothesis.

The bacillus of Klebs is ordinarily found on the free surface of the false membrane, but in some cases the most superficial layer of the membrane is covered by different forms of microbes in which the bacilli of Klebs nevertheless predominate. These bacilli are colored with methyl blue, reproduce themselves rapidly at a temperature of 33° C. on coagulated serum; more slowly on gelatin. The bacillus is about the same length as the bacillus of tuberculosis, but thinner, while its rounded extremities are more deeply stained than the middle part. It is movable, and rapidly reproduces itself in liquid media, while, when developed in fluid cultures, an acid reaction is developed, which finally gives place to an alkaline reaction. The bacillus of diphtheria may be preserved for months at a time, and cultures have been found virulent after five months retention at a temperature of 33°. When dried and preserved at this temperature they lose their virulence at about three or four months. The false membrane, however, preserves its virulence even after five months' desiccation. These facts are extremely important, and will explain many cases of the apparently spontaneous origin of diphtheria. Thus, Sylvestre, in *Le Progrès Médical*, 1890, pp. 353, 393, and 414, quoted a case of diphtheria in a young man, which developed a few days after contact with the clothing of his mother, who had died two years previously with diphtheria, the clothes having been kept during all that time in a closet, where the dampness and absence of light furnished the most favorable conditions for the preservation of the virus. So, also, a case is reported by Dr. Worms (*ibid.*), where diphtheria was produced by the use of an old camel's-hair brush, and the inquest demonstrated that five years previously this brush, which had been kept all this time wrapped up in paper, had been used in a case of diphtheria.

Another etiological cause to be considered in the study of the propagation is the fact that the diphtheria of the common fowl may be communicated in the most virulent form of the disease to man. Wolff (*Berliner Klin. Woch.*, 1883) and Wurdman (*Deutsche Med. Woch.*, 1886) have reported numerous cases of this character, while Delthill (*La Médecine Moderne*, No. 42, 1887), in a memoir read before the Académie de Médecin, reports fifteen cases coming under his observation, which seem to show in the clearest manner the transmission of diphtheria from animals, and above all from birds to man. So, also, Dr. Davidson (*British Medical Journal*, October 25, 1890) refers to numerous other cases where the same origin of the disease was probable.

It has, however, been proved that the bacillus of Klebs, or the diphtheritic virus, placed in contact with a perfectly healthy mucous membrane, does not provoke diphtheria, but that there must be some lesion or erosion to permit infection; consequently, the mortality of diphtheria is much more elevated in cold weather, and the researches of Bruhl clearly establish this fact. Thus, it results from statistics, the more uniform the temperature the less the mortality.

A point which at first excited considerable doubt as to the actual etiological value of the bacillus of Klebs was the observation made by a number of bacteriologists that this bacillus never invaded the different organs of the body, and was never found in the blood of patients or of animals inoculated with it, but was confined invariably to the false membrane. It is, therefore, not the bacillus itself

which produces the serious symptoms which characterize diphtheria, and it is now generally admitted that these symptoms are produced by a poison secreted at the point of infection by the bacillus, and carried by the general circulation into the system at large. This idea was first suggested by Loeffler, who considered the poison as a diastase, and his views were likewise investigated by Roux and Yersin, who were able to greatly extend our knowledge of the *modus operandi* of this bacillus.

A paper published in *La Tribune Médicale* for January 29, 1891, to which we are indebted for many of the preceding facts, is mainly devoted to an analysis of the works of these latter authors, who for the last three years have been incessantly occupied with the study of this subject. At first Drs. Roux and Yersin experimented with cultures sterilized by filtration through porcelain. In varying the dose in inoculation, under the skin or injected into the trachea or into the veins, they were enabled to produce either the death of the animal, or a characteristic diphtheritic paralysis, which sometimes was cured, or which sometimes led to the death of the animal. In the autopsy of all animals so inoculated, whether chickens, rabbits, guinea-pigs, or dogs, there were found the same lesions as occurred in animals inoculated with the cultures of the bacilli itself; the same œdema, the same indurated tissue at the point of injection, the false membrane only being wanting; consequently their experiment seemed to prove that some substance developed by the bacillus and its culture passed into the solution and was contained in the filtrate. Roux and Yersin also pronounced this poison as a diastase on account of the manner in which this filtered liquid behaved when exposed to the air and to heat, both of these agents appearing to diminish the virulence of the product in a marked degree. When evaporated, the filtered cultures left a dry residue, of which a part was soluble in alcohol and another part soluble in water. The alcoholic solution was free from all pathogenic properties. On the other hand, the aqueous extract was excessively toxic, and consequently contained the toxic principles. They also found that the diastase could be precipitated from the aqueous solution by a ninety per cent. alcohol solution in the filtered cultures or by the addition of lime or phosphate of calcium. In these cases the active principle adhered to the precipitate, and, introduced under the skin of animals, produced the same symptoms as the inoculation of the filtered cultures or the cultures still containing the bacilli. It is evident that these methods all indicate that we have to deal in such cases with something of the nature of a ferment. To obtain this diastase in a state of purity, recourse must be had to dialysis, since it also will pass through an animal membrane, and may then be obtained in a state of purity by dialyzing the filtered culture, which will still possess toxic properties.

These results as to the mode of action of these poisonous emanations from the bacilli have likewise been confirmed by Babes (*Virchow's Archiv*, Bd. cxix., 1890, p. 460), though he extended the matter still further by his success in the developing of false membrane and paralysis as the result of the inoculation with these filtered cultures. Brieger and Fraenkel (*Berliner Klin. Woch.*, 1890, Nos. 11 and 12) have, in addition, produced satisfactory proof of the fact that this poison secreted by the bacilli is not a ptomaïne and is not of a crystalline character. It apparently is more of the nature of a proteid, for, on saturating the bacillus cultures with ammonium sulphate, a precipitate is obtained which is insoluble in alcohol but soluble in water, and developing the biuret reaction for proteids. It is these authors who first introduced the name of "toxalbumen" as applied to this derivative of the bacilli, which they regard as a derivative of albumen, closely agreeing with serum albumen in its nature. When inoculated into animals, this substance is seen to be extremely toxic, is fatal in the dose of about $\frac{1}{25}$ grain for every two pounds of body-weight, while in smaller doses it produces the same phenomena and the same lesions as the bacillus cultures or those in which the bacilli are still present, although usually false membranes were absent.

Leaving now the considerations as to the pathology of diphtheria, we reach a stage of the question of more interest to the general practitioner,—that is, Can diphtheria be prevented? can animals and individuals be protected from its ravages? and can it be cured when it already exists? We here find numerous replies to these questions, all of great interest, all of great value, and many of great promise. It is further remarkable that so many different observers should be occupied with this question, and reach almost identical results by different methods. Among others the researches of Brieger and Fraenkel, Behring, Kitasato, Von Schweinitz, and Gray are especially worthy of notice.

Fraenkel (*Berliner Klin. Woch.*, 1890, No.

49), who is already known for work in this connection, for his determination of the nature of the filtered culture of the bacilli of diphtheria, tested a number of methods with the idea of determining immunity to the action of the diphtheritic poison, employing in the first place cultures of the bacilli attenuated in their virulence through the action of antiseptic substances and inoculations with the pure dried toxalbumen itself. These methods proving inefficacious, the toxalbumen was freed from organic germs by filtration or by heating to 55° C., and although he found that this procedure rendered animals less susceptible to inoculation with the bacillus of diphtheria, immunity was not conferred. Inoculation with large quantities of the bacillus culture liquid heated to 100° gave somewhat more satisfactory results, while when this bacillus culture liquid was exposed to a less temperature, about 65° to 75°, and then injected into guinea-pigs, the animals became slightly refractive to subsequent inoculations of the bacilli, provided two weeks was allowed to elapse between the injection of the culture and the inoculation with the bacilli. According to Fraenkel, the poisonous substance and the vaccine which confers the immunity, both of which are developed by the bacilli, are two distinct bodies, and he believes that the culture liquid, when employed as vaccine, at the temperature of 55° to 60°, weakens the action of the poisonous principle without affecting that of the vaccine; while the latter is destroyed by exposure to a higher temperature. Fraenkel thus has determined that it is possible to vaccinate against diphtheria, although his methods are of no therapeutic avail during the actual progress of the disease.

A decided step in advance has been reached through the reports of Drs. Behring and Kitasato, who, working in Koch's laboratory, announce results as to the production of immunity against diphtheria and tetanus, which would seem to establish beyond question the possibility of conferring absolute immunity against these two diseases, while they have also succeeded in curing animals suffering from diphtheria and tetanus (*Deut. Med. Woch.*, 1890, No. 49). The authors announce as the basis of this production of immunity that the immunity of rabbits and mice rendered refractory to tetanus depends upon the power which the blood possesses of rendering innocuous toxic substances manufactured by the bacilli of tetanus; and they find that the blood of rabbits rendered refractory to diphtheria possesses properties which enable it to destroy the poison of tetanus, and that these properties are located in the serum of the blood, a liquid deprived of all cellular structure. This property is permanent, and again reconfers immunity when transfused from animal to animal. Various methods were employed by these authors for rendering animals immune to diphtheria, and just as they found that the serum of the blood of protected animals destroys the poisonous principle of the tetanic bacilli; a similar method was found to govern the production of immunity from diphtheria. Certain animals, such as rabbits and mice, are naturally refractory to diphtheria, and may receive without harm injections of quantities of culture, which would inevitably prove fatal to much larger animals, such as guinea-pigs, rabbits, or sheep.

Dr. Behring describes four different methods through which the non-refractory animals may be vaccinated against diphtheria: 1. By the injection of bacillus cultures, which, after fourteen days, render guinea-pigs refractory to doses which would prove fatal to normal guinea-pigs. 2. The employment of trichloride of iodine added to an old culture in a preparation of 1 to 500. In these two methods it is the substance secreted by the bacilli, the living animal organism, which produces the immunity. 3. Immunity may also be produced by inoculating the products secreted by the bacilli in the living animal organism. For the purpose the authors used the pleural liquid collected from guinea-pigs dead from diphtheria. The inoculation of this exudation generally caused death; but when the animals survived they were then absolutely protected against diphtheria. A still fourth process consisted in inoculating animals with virulent cultures, and then controlling their deleterious action by appropriate therapeutic measures, a method the principle of which is the only one applicable to the treatment of this infectious disease in man. Dr. Behring found that there were a number of chemical substances, such as orochloride of sodium, naphthalin, trichloracetic acid, and phenic acid, which were capable of curing guinea-pigs affected with the poison, but the most active substance of all was the trichloride of iodine injected in one or two per cent. solution in amounts proportionate to the size of the animal. When the remedy and the poison were injected together, a circumscribed local inflammation was produced, followed by a slough, while

virulent diphtheria bacilli remained in the ulcer which resulted, and which lasted usually for three weeks after the operation. When guinea-pigs so treated are entirely recovered, or only show a superficial ulceration, it then becomes absolutely impossible to reinfect them even with inoculations of such virulence as would destroy unprotected animals in thirty-six hours. In rabbits, the trichloride of iodine acts even better, but it still seems improbable that this remedy can be employed in human therapeutics. In the first place, it is extremely caustic, and in the next place it does not give such striking results when the infection has taken place by way of the larynx or the trachea. The action of this remedy is, without doubt, its power of destroying the soluble substance secreted by the bacilli. Finally, Dr. Behring has found that a great resistance to diphtheritic infection may be conferred on guinea-pigs through the action of peroxide of hydrogen. This preparation is employed in ten per cent. solution, slightly acidulated by sulphuric acid. It is in certain cases a very energetic disinfectant, and Dr. Behring entertains great hopes as to its value in the treatment of diphtheria in man. Unfortunately, however, this method must be employed before inoculation, as when administered after inoculation with the diphtheritic poison its action seems to aggravate the intensity of the disease.

Through Behringer's researches, thus, we have found that animals suffering from mild diphtheria may be cured; but, unfortunately, the results are not applicable to human medicine. Dr. Behring's observations, however, mark a distinct advance over any other point of view; for, in the case of the iodine trichloride, there is no question of the establishment in the organism of a tolerance either of the bacilli or of their poisonous products, or of the antagonism of one to the other, the immunity being due to the presence of a chemical compound having nothing to do with the disease.

In that the direction of study has been so clearly established, and has been already so fruitful of valuable results, it is not expecting too much, then, to believe that in the near future some such positive preventive of this disease, which will be applicable to man, may be looked for; and, in a recent note, published by Drs. von Schweinitz and Gray, the statement is made that a substance has been obtained which renders guinea-pigs treated with it insusceptible to diphtheria upon the subsequent injection of strong diphtheritic virus into the circulation of these animals, while the test guinea-pig within forty-eight hours after infection died. These authors state their belief that the results of the studies in which they are now engaged will be available for the prevention and control of diphtheria in man. They have not, however, published a detailed account of their studies.

THE PROTECTIVE VALUE AGAINST SMALL-POX OF KINE-POX VACCINATION.

THIS question has again come to the front in consequence of an investigation which has been for more than a year going on by the British Royal Commission and the recent publication of the third report of this Commission.

There is a small but influential and noisy minority of scientific men, with some few prominent physicians in England, who are disbelievers in the protective power of vaccine inoculations. On the continent the anti-vaccinationists constitute a league, with its head-quarters in Paris, which publishes much matter in tract form for general circulation, and in various ways foments a public sentiment against vaccination. In this country the movement has never assumed large proportions.

The arguments against variola vaccination are presented at great length in a work published, in 1889, by Edgar Cruikshanks,—a work which has been styled "a most important addition to the vast literature of vaccination,"—"The History and Pathology of Vaccination." Dr. Charles Creighton is the author of the notoriously one-sided article on vaccination in the "Encyclopædia Britannica," and a still more recent article in the *Arena*. Briefly, the contention is this: "Vaccine disease is not a form of small-pox at all; it has nothing to do with small-pox, . . . being a strictly local ailment; whereas small-pox is an eruption of pustules all over the body, attended by a fever, and spreading by contagion. What nonsense to advocate the prevention of small-pox by the inoculation of a merely local malady of the cow's udder, which has nothing in common with small-pox except a superficial likeness of name!" An appeal is made to instances innumerable of the failure of vaccination to protect against epidemics of small-pox (see the official figures of the epidemic of 1874 in Bavaria, a thoroughly well-vaccinated country, where, out

of 30,742 persons attacked by small-pox in one epidemic, no fewer than 29,429 were vaccinated, and among the 4884 who died of small-pox, 3994 were vaccinated).

The advocates of vaccination base their belief in its efficacy on the results of the past century, since Jenner first promulgated his views and his painstaking test experiments. They believe that the protective benefits of vaccination have been sufficiently proved by experience. Before Jennerian vaccination came into vogue small-pox was one of the most formidable scourges of the human race, causing a mortality of ten per cent. Since the general adoption of vaccination by civilized nations, the mortality from small pox has been reduced to a very inconsiderable figure (less than one per cent.). There have been epochs and places when, during the prevalence of small-pox, the enforcement of efficient vaccination regulations have been followed by a stamping out of the epidemic. Facts and figures to prove this are abundantly at the command of the vaccinationist, and they have been feebly met or ignored by the opponents of vaccination.

Another line of argument, based on incontrovertible facts, has been especially convincing to the unprejudiced, and cannot be easily met by the men with the antivaccination bias. Side by side in a nation you may have one set of people who have been poorly or not at all protected by vaccination, and among these the small-pox will rage with great fatality, and another set, all of whose members shall have been the subjects of enforced vaccination, and scarcely one of the latter shall be touched by the epidemic. This was the case with the Prussian army during the small-pox epidemic, which, from 1857 to 1861, spread over all Germany, and caused among the civil population nearly eight thousand deaths. The mortality in the army, where vaccination and revaccination had been rigidly enforced, was practically *nil.** This seems to be a sort of test experiment on a large scale, for camp and barrack life has generally furnished excellent conditions for the spread of small-pox. Bouley† affirms that "the same results may be observed to-day in our [the French] army. Since revaccinations have been practised there with great regularity, and since care has been taken to procure by a revaccination of urgency, the immunity of soldiers in all localities where small-pox rages among the civil population, the contrast is strikingly and absolutely demonstrative, . . . the mortality among the military being almost nothing." A contrast of a similar kind is alluded to by Bouley between the mortality from small-pox during the Franco-Prussian war, of the French army (unvaccinated) and the German army, where vaccination had been made obligatory.

We have no space for the elaborate statistics compiled several years ago by Dr. Martin, of Roxbury, showing the average annual mortality from small-pox among the different nations of Europe for various decades before and since the introduction of vaccine. Thus, in one department—that of the province of Trieste—the deaths from small pox alone were 14,000 per 1,000,000 of inhabitants during the period of thirty years just before the introduction of vaccine, and only 182 during the period of forty-two years which followed the practice of vaccination!

To statistics of this kind the antivaccinationists oppose the failures of vaccination, and never in any instance hint at the possibility that these failures to protect (which admittedly have been sufficiently numerous) were owing to the bad quality of the vaccine matter employed. Every physician who has been in active practice during the last forty years well knows to what those failures may be attributed. He remembers the time when he himself saw reason to lose faith in the Jennerian vaccine, transmitted from arm to arm for countless generations, till, by the feebleness and want of typical characters of the local and general reaction, it seemed to him to have become literally an "attenuated vaccine." He remembers well his own frequent mistakes in using dried scabs for vaccine matter (taken from the arm of some patient) instead of the clear lymph, which oozes from the primary vesicle about the seventh day, and admits that in some instances he may have communicated to his patient by the employment of these crusts a mild form of septicæmia instead of the cow-pox disease. He admits also the possibility that in rare cases (as the antivaccinationists affirm) "humors," even syphilis, may have been imparted through the use of faulty (humanized) vaccine. All this, however, the physician of forty years or more of experience in vaccination attributes to ignorance; and his faith in the almost absolute prophylactic efficacy of animal vaccine of a pure quality (the pure watery lymph of the primary vesicle, devoid

* Leon Collin, "Traité des Maladies Épidémiques."

† "Le Progrès en Médecine par l'Expérimentation," p. 261.

of all admixture with blood or pus) receives confirmation every day.

In reading the recent writings of the leading antivaccinationists (Cruikshanks, Wallace, Collins, Picton, Creighton), we have been struck by the utter lack of appreciation of all that has been contributed to science during the past twenty-five years respecting the comparative pathology of infectious diseases, the nature of virus, of attenuated virus, etc. Considering the modifications which virus often undergoes in the animal economy and the more powerful resistance and reaction which the animal often presents to the infectious agent, transplanted by inoculation from the human subject (in some animals, for example, all attempts to inoculate tuberculosis fail, and most animals prove refractory to syphilis), it would not be beyond the *possibilities* that the vaccine disease *may be* a modification of small-pox, although Charles Creighton declares that it would shatter any man's scientific reputation to affirm it. We regard the latter and all the clique which he represents as equally rash and foolhardy in their reiterated declarations (based on nothing but assumption) that there is *no* identity, consanguinity, or likeness between variola and vaccine; we ourselves are content to remain in a state of suspended judgment on that point, though satisfied that the findings of the Lyonese Commission cannot be regarded as the final word on that subject.

Since the above was written our attention has been called to some new researches on variola vaccine, which, if they shall be confirmed, will settle the contention forever by establishing the unicity of cow-pox and small-pox. Haccius, director of the Vaccinal Institute of Geneva, and Eternod, Professor of Histology in the Geneva School, following the operative method of Fischer, as described in the *München Medicinische Wochenschrift* last year, claim that they have succeeded in imparting small-pox to animals, and in transmitting it through several generations, the disease eventually manifesting itself in a mild form, indistinguishable from true cow-pox, and, like the latter, conferring immunity from variola.

"Believing that the method of inoculation by pricks and incisions, practised by the Lyons Commission, was insufficient, and that experiments based upon this method were inconclusive, these later experimenters have resorted to a method that they call *vaccination on surface, or vaccination by denudation*. They denude the skin of the animal over an extent of several square centimetres by means of a thin glass scraper. . . . Then they rub the denuded surface with a spatula charged with the small-pox virus. They assert that by this procedure they have never failed to obtain success, while the method of pricks and incisions is very apt to fail."

The first products of this method of vaccination appear to have been a local eruption of papules of little typical character, "abortive," like those "which led the Lyonese Commission into error." If from the product of these papules another series of inoculations be practised, and a third from the second, "the pustulation tends to become typical by taking on more and more the mode of evolution and characters of the vaccinal eruption." After the third generation the pustules "cannot be distinguished from those obtained in the vaccinal institutes by the inoculation in the first generation of spontaneous cow-pox."*

Among the conclusions stated by these experimenters is the one which, if established, must henceforth silence all cavils and objections,—that "small-pox, inoculated in the heifer, becomes transformed into vaccine in the course of several generations by transmission through this animal. Duality is thus disproved."

THE TREATMENT OF LUPUS BY KOCH'S METHOD.

THE surgeons of a past age were well acquainted with the anatomical features and pathological results of lupus; thus we find in "Cooper's Surgical Dictionary," published in 1802, this description: He calls lupus by the name now gone out of vogue, *Noli me tangere*, and defines it (substantially) as a slow tubercular affection, occurring commonly about the face, having a tendency to end in ragged ulcerations of the cheeks, forehead, eyelids, and lips, and sometimes appearing in other parts of the body, where it gradually destroys the skin and muscular parts to a considerable depth. The disease is said "to begin in small tubercles, which change after a time into superficial spreading ulcerations more or less concealed beneath furfuraceous scabs."

The true nature of tubercle long remained in obscurity. It was regarded as scrofulous, then as syphilitic; good authorities took the

* *Boston Med. and Surg. Journ.*, January 22, 1891.

view that it was invariably of syphilitic origin. Thus, Dr. Clement Lucas, writing in the London *Lancet* in 1879, says, "It is not too much to affirm that nearly every case of extensive ulceration of the face, to which the term *exedens* might with good reason be applied, has its origin in syphilis. Erasmus Wilson, in his "Diseases of the Skin" (1860), favors this view.

Friedlander and Koster were among the first to show the morphological identity of lupus with tuberculosis, and Koch's subsequent discovery of the bacillus tuberculosis in lupous tissue, and the striking experiments of Schüller and Huber seem to have established the tuberculous nature of lupus beyond cavil or question. The arguments for this view are well stated in the article by Neisser, "On Chronic Infectious Diseases of the Skin," in Ziemssen's "Hand-Book of Diseases of the Skin."

If we were to sum up the history and course of lupus from its inception, we might say that the doctrine now held is that there is first penetration of the derm by Koch's bacillus. The bacillus acts first on the walls of the blood-vessels of the part producing that damaged state which is the anatomical substratum of inflammation; there is a migration of leucocytes into the meshes of the surrounding connective tissue. The irritation of the bacillus causes these migrating corpuscles to assume a variety of developmental forms, chief among which are those known as "giant cells." The agglomeration of these exudation cells constitutes the tubercle. Delicate blood-vessels permeate the tumor; these soon become choked out by the luxuriance of the growth, and there is caseation (by starvation) in the centre; this was the older view. It is now taught that the caseation is a coagulation-necrosis, caused by the poisonous character of products engendered by the bacillus itself. While the growth dies at the centre, it extends peripherally, and simultaneously the necrobiosis spreads, and thus we have the characteristic feature of this disease,—"formation and disintegration of the nodules under the influence of a virus, spreading into the periphery." As the nodular masses all perish one after another, "not only the first attacked portion of tissue is destroyed, but likewise its surroundings, which coalesce with the new formation, both in width and depth, and perish" (Neisser).

Hebra has greatly simplified the nomenclature of lupus by showing that the many varieties described by authors under the terms tumidus, exedens, non-exedens, exuberens, rodens, exulcerens, exfoliativus, fungosus, serpiginosus, etc., "are all simply differences in the stage, position, or mode of development of the same disease," which he calls lupus vulgaris.*

Koch's remedy, concerning which so much talk is now being made, is stated by him to be a glycerin extract, derived from the pure cultivation of tubercle bacilli. According to his explanation, this extract, when injected into the system, precipitates in the environment of the tuberculous nodules the changes which are effected in the centre of the nodules under the influence of the bacilli themselves, a coagulation-necrosis, which stops the further spread of the tuberculous growth.

"The tubercle bacilli produced when growing in living tissues, as in artificial cultivations, contain certain substances, which variously and notably unfavorably influence living elements in their vicinity. Among these is a substance which, in a certain degree of concentration, kills or so alters living protoplasm that it passes into a condition that Weigert describes as coagulation-necrosis. In tissue thus become necrotic, the bacillus finds such unfavorable conditions of nourishment that it can grow no more, and sometimes dies."

In other words, that which is a natural effect of the bacillus when developing in a tissue, stopping short of completeness owing to the existence of new breeding-soil for the bacillus at the periphery of the nodule, Koch attempts to reinforce and heighten by artificially increasing the amount of necrotizing substance in the vicinity of the bacillus, thus destroying the conditions of nutrition for the bacillus.

As for the results of this new treatment, it is still too early to pronounce definitely. Numerous cases of lupus so treated are reported as cured; in others, marked ameliora-

* "Since Willan and Bateman at the beginning of the century attempted to restrict the term lupus to particular ulcerations about the face, an almost innumerable series of varieties have by various writers been described, and many divisions have been suggested, according to the stage or condition of the lupous process. But the division which has taken most hold on the profession is that of Rayer into *lupus exedens* and *lupus non-exedens*. This was generally accepted by the profession, and became the basis of clinical teaching. Against the continuance of these terms I wish most emphatically to protest, and I trust that they may soon be considered as much out of date as the still older *noli me tangere*. Apart from their general awkwardness, they simply express stages of a process, or differences in the rate of progress of the disease."—R. Clement Lucas, in London *Lancet* (American reprint), 1879, p. 289.

tion has been noted. Will the benefit be permanent? We must wait and see. Perhaps the estimate of Kaposi (who is so good an authority on lupus and allied destructive formations) may be taken as fairly representing the present status of science on this question.

At the recent meeting of the Imperial and Royal Society of Vienna, Kaposi reported that he had subjected in all thirty-two patients to this treatment. These patients had now remained under observation about six weeks. He presented at the meeting six cases, which were apparently cured; the skin was everywhere smooth; nowhere was tubercle or ulceration perceptible. He has found that at the end of a certain time the extract produced by the bacillus (Koch's *mittel*) no longer acts in small doses, the dose must be augmented. In a certain proportion of his cases he interrupted the treatment for several weeks; then he recommenced with small doses, on the supposition that the bacilli had acquired a new vitality. He invariably found that there was a new reaction to the injections, as if the bacilli had only been overcome for the time,—driven into latency, not destroyed. In some of these patients the interruption was actually followed after a time by a reawakening of morbid action at the seat of the lupus and by the formation, in some instances, of new foci of disease. "We turn," he says, "in a vicious circle. On the one hand, we exercise a favorable action on the lupus by means of the injections; on the other, the interruption enables the lupus to continue its development, and as the bacilli cannot be eliminated from the tissues, they may penetrate the lymphatic ducts and provoke metastasis. The problem, then, is, how to favor the elimination of the bacilli. The thermo-cautery and the cutting curette will remain indispensable in the future." Kaposi might, perhaps, have added the arsenical paste, so popular with the old surgeons, and so often successful under careful management.

At the same meeting, Billroth mentioned the case of a lupus patient who had lately been sent to his surgical clinic to have the operation of rhinoplasty performed. He was supposed to be well, but the upper lip was still hard and infiltrated. This infiltration disappeared after several injections. In this patient an interruption of twelve days was made in the treatment; then a moderate dose was injected, and the reaction was intense. Afterwards an injection of 15 centigrammes was made, and there was no reaction. In another case of lupus, there was an extremely violent reaction. During an interruption of a fortnight, the lupous lesions again broke out, being in full efflorescence.

The above shows the uncertainty in which the profession must for some time remain as to the permanently curative benefit of Koch's remedy in external tuberculosis, however striking may be the immediate amelioration.

Jonathan Hutchinson has lately concluded a series of interesting lectures on the "Nature and Treatment of Lupus" (*Lancet*, January 17, 24, 31). His views are not precisely those above stated. He contends that lupus processes of inflammation originate in persons who are locally or constitutionally of feeble cell-nutrition and prone to vascular disturbance. That a parasitic bacillus attends many of them is to be freely admitted; that its implantation constitutes the initial stage of lupus he gravely doubts.

He accepts the word lupus as the family name of a variety of maladies known as rhino-scleroma, lymphangeioma pigmentosum, lupus erythematosus, lupus vulgaris, scrofulo-dermata, etc., which all have these features in common. They attack chiefly those parts of the surface of the body which are exposed to the influence of cold and irritants, and they occur by preference in those who are by inheritance or acquisition of feeble organization, and who are proved to be in greater or less degree liable to the attacks of the tubercle bacillus. They are all developed most commonly in the period of adolescence. They are all infective in their local qualities, and continue to spread slowly for an indefinite number of years; and it is possible in every one of them that, after prolonged duration as a non-malignant chronic inflammation, a tendency to cancer may be shown. Every one of them disorganizes the tissues which have been affected by it, and leaves behind it a scar. Concerning almost all of them, it is freely admitted that syphilis may produce very close simulations, and at the same time it is denied that their type forms have any connection, remote or otherwise, with such taint. With the exception of only the most erythematous forms of erythematous lupus, destruction by local measures of the infective material is required in every case, and without any exceptions at all, attention to the general health by the use of a liberally tonic regimen is requisite, together with the protection of the parts from all external irritation, and more especially from cold.

Among the local measures of treatment he gives his preference to the actual cautery and the acid nitrate of mercury. He speaks favorably of erosion by Volckmann's scoops. Instead of Dupuytren's (arsenical) paste, he uses the liquor arsenicalis, which may be painted on with a camel's-hair pencil. Undiluted carbolic acid is very efficient, and if the patient be intelligent, he may be trusted to make the applications.

With regard to Koch's treatment, he is very guarded in pronouncing an opinion. The cases which appear to derive the greatest benefit are those in which there is most of inflammatory swelling, and in which the more specialized elements of the lupus process are least abundant. In lupus erythematosus, the injections seem to have failed. They have not yet, he says, been tried in cases of perfectly quiet lupus,—*i.e.*, single-patch lupus occurring on the cheeks of healthy persons, characterized by a thick growth of "apple-jelly," and by the entire absence of any surrounding inflammation. He believes that such cases would not be benefited by the treatment. We are obliged, he says, to report that nothing that can be called a cure of lupus by the new treatment has yet been obtained in London practice. The patient, who was taken to Berlin by Mr. Malcolm Morris and Dr. Pringle, and was for a time supposed to be almost cured, is now said to be in a condition almost as bad as before the treatment. From all quarters we hear of relapses occurring quickly.

It may be, however, that in the future this method of treatment may be put to some use, especially if combined with the older methods of destruction of the lupus deposit by means of cautery or caustic. The ill effects of the treatment on the general health soon seem to pass away. When febrile reaction ceases to occur, it seems evident that there is no longer hope that the lupus nodules will be attacked.

TREATMENT OF TUBERCULOSIS BY TRANSFUSION OF BLOOD FROM AN ANIMAL REFRACTORY TO TUBERCULAR INFECTION.

FOLLOWING the example of Koch, numerous bacteriologists have endeavored to so modify cultures of the tubercular bacillus as to obtain a vaccine which would be efficacious in the tubercular process. An entirely new point of view has, however, been reached in the line of study opened by Drs. Richet and Hèricourt, who have endeavored to confer on an animal liable to tuberculosis a more or less marked degree of immunity to tubercular infection by the transfusion or introduction into the economy of the blood of an animal refractory to tuberculosis. The results of these experiments were announced at a recent meeting of the Société de Biologie (*Gazette Médicale de Paris*, January 24, 1891).

These authors claim that the transfusion into rabbits of the blood of the dog, or, even better, the peritoneal infusion, which permits of much larger amounts being employed, attenuates and retards in these latter animals the evolution of tuberculosis, and that this can again be rendered more intense and more manifest by removing blood from a dog which had previously been inoculated with a certain quantity of very active tubercular virus. The authors appear to have employed no such line of experimentation on man, although they claim that they intend to carry out such a line of study, as, if conducted with prudence, it is free from danger. Among the animals refractory to tuberculosis, whose blood may be utilized in this method of treatment, are the dog and the goat, and the statement is made that Dr. Lépine has already injected from 1½ drachms to 3 ounces of the blood of a goat into the cellular tissues of patients affected with tuberculosis without noting any local or general action, with the exception that in two cases there was slight painful swelling at the seat of injection, which lasted for one or two days. An important addition to this observation is the statement of Lépine that it is not necessary to inject the entire blood, but that the serum is quite as efficacious. It is evident that, if this is a fact, one serious source of danger is avoided, for, as is well known, the transfusion of blood of one species of animal into the veins of another is apt to lead to the destruction of the red corpuscles, and the production of hæmoglobinuria and other serious accidents; and the statement is made that Drs. Richet, Lépine, and others have injected subcutaneously into tuberculous patients, with perfect harmlessness, 15 to 30 drops of the serum of the dog.

This experience has been repeated apparently sufficiently often to prove its entire freedom from danger. Its therapeutic value is not, however, so clearly established; for, in the first place, admitting the value of the statement that the blood of an animal refractory to tuberculosis might give immunity to tuberculosis, the question is, what animal

should be selected, since, as is well known, the immunity of the dog to tuberculosis is only relative? and at the meeting of the Société de Biologie, January 17, 1891, Dr. Roget showed specimens from a dog dying from pulmonary tuberculosis. The pleura of the animal was considerably thickened, and in the lungs there was a small caseous pneumonic nodule containing micro-organisms which gave the same reactions as the tubercular bacilli, although more slender and longer than those found in man. This dog had been infected with tubercular meat. Dr. Richet's method of preparing the serum of a dog is to place a canula in the carotid (*La Médecine Moderne*, January 22, 1891), and then collect the blood in a sterilized bulb, in which it is allowed to coagulate. When the serum separates, it may be readily collected by means of sterilized glass tubes, whose extremities are then sealed hermetically. The authors state that they have performed seventy-five injections without ever having the slightest accident of any kind.

Lépine, however, has shown experimentally that this immunity is enjoyed to a greater degree by the goat, and he announces that he is now conducting a series of experiments, whose results he promises shortly to publish.

Reports on Therapeutic Progress.

A CRITICAL STUDY OF KOCH'S CURE FOR TUBERCULOSIS.

PROFESSOR SEMMOLA publishes in the *Internationale Klinische Rundschau* for January 4 and 11, 1891, a criticism of Koch's method of treating tuberculosis, which may perhaps, now that the wild enthusiasm has somewhat abated, receive the attention which the author's reputation as a careful clinician warrants. We do not pretend to endorse all Professor Semmola's views, but we cannot but believe that much would have been avoided had his beliefs been more generally held.

"In the midst of the universal enthusiasm aroused by the discovery of Robert Koch, it may seem strange and presumptuous if I venture to express very grave doubts respecting the therapeutic value of Koch's cure for tuberculosis, my judgment being based upon clinical observation and upon the incontrovertible data of rational therapy. Months, perhaps years, will pass,—unfortunately no mortal can measure the duration of such sad delusions and fashions, especially in the province of medicine,—but the truth will at last prevail.

"When it shall have been the special purpose of one's life, during a long series of years, as it has been of mine, to harmonize the disclosures of the laboratory with the results of clinical therapeutics, it will be seen that by depending on that strong experimental logic which should always guide the biologist, as well as the physician, in the laboratory or at the sick-bed, I have been rendered unable, to my great regret, to participate in the universal enthusiasm, despite my high esteem for the great Berlin investigator.

"When, in the year 1880, the investigations of Pasteur were made public, respecting the immunity achieved by inoculation of diluted virus, I was very sceptical as to the value which Pasteur placed upon the utilization of his method in practice.

"I forbear any reference to the comical aspect of the question. The pen of a Molière would be needed to portray this 'progress' in modern medicine, representing a man in sound health, who, for the purpose of obtaining assured immunity from the virulent germs of the external world, subjects himself to a series of antidiphtheritic, antityphus, antiscarlatinous preventive inoculations, thus producing in himself a series of artificial diseases.

"For my part, I must openly confess that I fail to see this remarkable progress, and it seems pertinent to ask whether all these attenuated poisons, introduced successively into the organism, would possess the same preventive power as if only a single one were employed for inoculation.

"Naturally, if such progress were possible, a much smaller number of people would be carried off by death, and the conditions of existence would be withdrawn from a large number of the lower or invisible forms of life,—a contingency for which scarcely any one would grieve, as men would thus be less tormented by microscopical parasites, although the latter, on the whole, are the least dangerous.

"But the sad consequence would be that our planet would soon become overpeopled, and the social problem, which to-day is the subject of lively discussion, would grow more grave and terrible in character, for the danger would arise that men, liberated from the invisible parasites by the progress of medicine, would become all the more the prey of the macroscopic parasites, against which, un-

happily, there are no preventive inoculations. Then there would prevail a veritable moral anthropophagy, with all its consequences!

"On the occasion of my visit to London, during the meeting of the International Medical Congress, in August, 1881, I took part in the *fête* given by Lord Granville in honor of the members of the Congress. I was there a witness of the boundless joy with which the mothers present greeted the promises of Pasteur, placing in early prospect a future when, thanks to preventive inoculations, infective diseases, such as scarlet fever, diphtheria, etc., would lose their dangerous character. Though it caused me pain to rob them of their illusions, I could not help declaring straightway, what I had often said and written,—namely, that those promises were the phantasies of a man who, unfortunately, is no physician, and accordingly not in position to comprehend the wide chasm which separates the laboratory of the biologist from the clinic. My views were justified by the facts, for these hopes continue to remain dreams.

"The praiseworthy zeal with which a large number of chosen spirits have followed the example of Pasteur has undoubtedly been crowned by brilliant triumphs in the current progress of biological methods; I must, however, declare that these triumphs, in their practical application to man for the prevention and cure of virulent and contagious disease, have proven worthless, and will so continue in the future. The cause is very simple:

"The impetus given to these investigations and expectations proceeded from an error in natural philosophy or experimental logic; accordingly, 'False premises, false consequences.' In truth, all these investigators were animated in their labors by the fundamental idea that Jenner's vaccination is a wonderful instance of immunity from small-pox, obtained by means of the inoculation of the virus of cow-pox, which, in their judgment, represented the small-pox poison attenuated in passing through the organism of the cow.

"This example, however, has nothing in common with the artificially-produced vaccines of Pasteur and his associates. I was always of the opinion, and still believe, that there is a great difference between these two things, and to those who believe differently I would here remark, that experiments and discussions have been going on for forty years, with the most contradictory results, and that thus far no conclusions have been accepted. We may therefore well ask whether sound experimental logic will permit us to proceed from the unknown and to make a leap into the future.

"Had I busied myself with these studies, I should have pursued a different course. First of all, I should have determined whether Jenner's vaccine really represented the attenuated virus of small-pox, and only after determining this would I have concerned myself further with the various other virus dilutions. But my experimental logic would not have made a halt here.

"I cannot admit that it is all one whether we obtain the dilutions of a virus through its introduction into the organism of another animal species, or through physical and chemical means, such as all the experimentalists have employed during the past ten years. *In this procedure I see a serious violation of the experimental method*, and until proofs of the contrary shall be adduced, I shall cling to the belief that it is one thing to dilute a virus in the living body and a very different thing to attenuate it by hydrochloric acid or heat. I have repeatedly pointed out that just such deviations from the experimental method are the cause of certain absurdities in contemporary medicine, which possess the appearance of earnest and precious acquisitions.

"Not only this error in experimental logic, but a further and not less serious illusion is to be observed.

"The vaccine of Jenner (which in reality is an unknown thing) is given to a healthy man in order to render his organism capable of resisting small-pox, or, in modern parlance, to render him immune from the development of the variola germs. But, I ask, what has this form of immunity or non-receptiveness to do with that other form which we wish to impart to the organism already diseased? and as such we must doubtless look upon an organism in which the poison already circulates (for example, after the bite of a mad dog). The thought of these alleged discoveries, which not long ago filled the whole world with enthusiasm, comes to me like a dream. Truly, if the 'progress' fever so intoxicates our senses, so blinds us, that we renounce the principles and the fundaments of the experimental method, and no longer distinguish white from black in the various experiments, arbitrarily modifying the conditions of the phenomena, and, in the name of experimental medicine, deducing more baneful

conclusions than can be charged to the old-time empiricism, I would earnestly implore that a halt be made! In the face of this feverish haste, I recommend that we turn about, and again traverse the path of this so-called progress of the last decade with the illuminating torch of that severe scientific logic which has guided so many great minds (especially at the beginning of this century) to the discovery of immortal truths, which then formed the basis of current progress in medicine.

"What analogy, I ask again, is to be found between the first and second form of immunity? Is it possible to believe that an organism into which the morbid poison has already penetrated calmly waits for the prophylactic or curative effect of the attenuated virus? I do not believe it at all, but must rather assume that as soon as a virus from without secures lodgement in the body, the chemico-biological relations of this organism are modified every minute, every hour, every day. Thus is inaugurated that slow, dystrophic activity which so disturbs metamorphosis that at a given moment the outburst of the clinical form peculiar to that virus must inexorably follow. In the present case, hydrophobia would inevitably develop. We know that a single drop of water is sufficient to cause the overflow of a liquid. This statement is an incontrovertible truth, acquired through the effective progress of physiology and general pathology.

"I cannot comprehend how true clinicians can believe in the practical value of the preventive or curative effects of attenuated disease-poisons, the virtue of which has been established solely in the laboratory; such is their belief, if the doctrine in question has once been established on hypothetical bases!

"The basis of my conclusions has been the investigations of Pasteur, not because Koch's liquid is an attenuated virus, but because the labors of Pasteur prepared the field for the investigations of Koch. Even now, if the 'lymph' of Koch, which is said to be a certain remedy for tuberculous affections, must be regarded as a further confirmation of the mighty impulse given by the labors of the laboratory, it nevertheless presents to the eye of the unprejudiced physician the same deficiencies, if not greater ones, as the other conclusions deduced from animal experiments and applied straightway to human beings.

"At this point I ought to discuss the reality of the primary claims made for the Koch 'lymph,'—that is, its alleged specific elective action on the tuberculous tissue. According to Koch's own reports, this elective specific action upon the tubercle is not to be questioned, for it is not to be assumed that an investigator like Koch would have made such a claim without being assured of his case and without having irrefutable proofs in hand. I will, therefore, not enter into a further discussion of this preliminary claim. I will also refrain from questioning whether this action is really to be regarded as an elective biochemical one, or only as a curative effect of the general hyperthermia and local hyperæmia which usually follow the injection of the Koch liquid. In truth, the clinic can report many instances of the cure of several local disease processes and hyperthermic influences, which accompany acute transitory disease. These curative effects, however, appeared to be as inscrutable as they are unstable, and accordingly may lay no claim to the designation of cures.

"I will even assume as true and firmly established this destructive influence upon tuberculous tissue. But, in order to cure tuberculosis of the lungs, we must, above all things, influence and heal the pretuberculous stage. The Koch 'lymph' cannot, and never could, exercise any modifying influence upon that deep-seated alteration of metamorphosis which leads slowly, and often only after the lapse of many years, to the tuberculization of the organism. This anatomical, pathological, and clinical knowledge with respect to tuberculosis, in connection with the special biological action of the Koch 'lymph,' afforded my chief grounds for denying to the discovery of Koch any success as a cure for tuberculosis of the lungs. I have, accordingly, not hesitated to openly express my opinion as a physician at a time when a foolish infatuation possessed the entire world.

"How could so many prominent physicians become enthusiastic over this supposed antituberculous remedy, inasmuch as the Koch 'lymph,' at the best, was incapable of removing the last anatomical consequences in a consumptive?

"All the more singular and incredible appears the joy of those who cling to the bacillary origin of tuberculosis, inasmuch as Koch's remedy cannot destroy the bacillus. I can, therefore, not refrain from mentioning that the enthusiasm of these gentlemen involves a peculiar contradiction, since they admit the possibility of a cure by means of a substance which does not kill the Koch bacillus.

"Whether adhering to the old or the new

pathogenic doctrine respecting tuberculosis, we cannot escape this dilemma. In order to cure tuberculosis we must either render the propagating soil (organism) unfit for the development of the tuberculous germ, or we must kill the bacillus itself. The Koch 'lymph,' however, is incapable of accomplishing either the one or the other. This conclusion must force itself upon the most blinded, if they are true physicians and investigators. Koch has himself declared that the 'lymph' is not capable of destroying the bacillus, and further words on this subject would seem superfluous. It would also be idle to speak of the heart-rending struggles of the tubercular bacilli, as they have been described by several observers, for, as Cornil properly remarks, these effects of the Koch remedy on the bacilli are creatures of phantasy.

"There accordingly remains to be mentioned only the action of the Koch 'lymph' upon the propagating soil (organism); that is, upon the organic disposition (whose nature is unknown to us) upon which the bacillus may thrive. The well-founded conjectures respecting the chemical nature of the Koch 'lymph,' as well as our previous knowledge of its biological effects, are more than sufficient to impart the conviction that, in view of the laws of experimental pharmacology and clinical therapy, the 'lymph' cannot possess the property of producing in the organic disposition to which we have referred the necessary beneficent modifications; and only a momentary forgetfulness of these principles has occasioned illustrious clinicians to greet this questionable discovery with enthusiasm. On the basis of the foregoing, I considered myself justified, a month ago, in delivering an unfavorable judgment upon the possibility of curing tuberculosis of the lungs with Koch's remedy. My judgment, thus respectfully expressed, aroused an echo that surpassed my modest expectations, for it was telegraphed to all parts of the world. I must assume that this unusual and unsought for publicity is to be ascribed altogether to the dangerous character of the disease which it was hoped to cure, and had no reference to my personality; for I could lay claim to nothing more than the rather bitter service of having possessed the courage to express my adverse opinions at the moment when the world was all applause. But, perhaps the expression of my own judgment on this subject was a treason? Is our freedom of thought to be prohibited when one has the fortune or misfortune of seeing what others do not see? Or, has Filicaia's utterance with respect to Italy remained true,—'Thy destiny is to remain ever a slave, whether conquered or victorious!'? Unworthy insinuations, open insults, and denunciations have been heaped upon me in the interval.

"But enough of these contemptible matters. Let us return to an unprejudiced scientific discussion, in order to see how it is that the biological action of the Koch 'lymph' does not permit our attributing to it the power of so modifying the biochemical constitution of the organism that it will lose the power of propagating the tubercular bacillus. The specific elective action of the 'lymph' is said, as is well known, to be directed against the tuberculous tissue, destroying by a special process (to discuss which in a scientific manner I look upon as altogether premature) all, even the most remote, tubercular gatherings, wherever they may be found in the lung. As I have indicated in the foregoing, this destruction cannot be regarded as equivalent to the cure of tuberculosis of the lungs, for after the destruction of the morbid tissue in one case, under the influence of the generally morbid condition, which remains unchanged, and of the bacilli which are not destroyed, other morbid tissue would be formed. Accordingly, looked upon from this point of view, the action of the Koch 'lymph' can never be regarded as equivalent to cure.

"In view of these principles,—as certain as mathematical demonstration,—it is only to be wondered at that any physician of scientific culture can persist in his enthusiasm after Koch's official report of the 13th of November last. I must assume that a very natural eagerness to liberate humanity from the terrible scourge of tuberculosis was so passionate and irresistible that it overcame the protests of sober reason; or, on the other hand, it must be assumed that Koch's 'lymph,' though failing to destroy the bacillus, possesses a biological action which modifies the organic conditions favorable to the reception of tuberculosis; so that in a measure it would seem as if Koch meant just this when he declared that he believed his 'lymph' to be a certain remedy for the cure of the initial stage of consumption. But, in all truthfulness, what is meant by the initial stage? What clinician, however distinguished, if he would be conscientious in his work, will venture to set exact boundaries to the evil?

"In the most charitable of interpretations,

we must accordingly reach the assumption that Koch's 'lymph' possesses the power of curing that terrible degeneration of the organism which affords an entrance to tuberculosis. In my judgment it would be simply a sign of great innocence to lull one's self with earnest hopes in this respect, for the form and manner in which the biological action of the Koch 'lymph' is developed does not admit the assumption that it possesses that slow and specific biochemical action on metabolism which is requisite in order to produce a radical modification in those slow and characteristic abnormal processes of metamorphosis which precede the formation of the tubercle.

"Such slow modifications of metamorphosis can in general be effected only by long-continued hygienic influences, or through certain mineral medicaments, such as mercury, iodine, and others, which, by means of an unknown chemico-mechanical action,—perhaps, as a result of the combinations which they form with the albuminoids,—prove compatible with the life of the organism on the one hand, without causing any visible disturbance; and, on the other hand, if their application be long continued, unnoticeably modify the direction of the nutritive function, so that, as a final result, cure of syphilis, scrofula, etc., takes place. But let it be noted that this special biological action is vested in mineral remedies alone, which, administered in moderate therapeutic doses, possess the property of long remaining in the organism, during which period they modify the cell-functions through chemical processes which are brought to bear on the new nutrients coming from the external world, without ever producing toxic phenomena. If such phenomena appear, the treatment must be terminated or retarded.

"Accordingly, for the purposes of scientific pharmacology and rational therapy, the toxic action, in the true sense of the word, stands in contrast to the property of a medicament which is supposed to possess curative power, and which is intended to modify continuously and permanently the nutritive activities of the sick organism. I should not be able to harmonize these two modes of action without setting up a pharmacological paradox. The reason is very simple. A substance which, in order to exercise this modifying power in the manner indicated, must produce toxic symptoms after each administration, cannot pass muster in my eyes as a curative agent; during weeks and months it would incessantly expose the organism to the dangers of repeated poisoning,—every day, every second day, etc.

"The conclusion is clear, and for this reason the slow modification of metamorphosis must remain the exclusive property of mineral medicaments, for, as stated, they are the only ones which, partly through chemical combinations, which they form even in small doses, partly because the organism will readily tolerate these doses for months without poisonous symptoms, will yield the physician in certain chronic diseases the most brilliant curative results.

"This mode of therapeutic action will never be achieved by organic medicaments, least of all by alkaloids, because, instead of acting from the very beginning through the biochemical mechanism peculiar to the mineral medicaments on the activities of metamorphosis, they reach the histological, muscular, nerve, or gland elements, producing at once more or less severe disturbances of function. Precisely these local disturbances of function produce in the general nutrition profound modifications as soon as they reach the degree of toxicity, and in this case they cannot possibly accord with health and life.

"When, however, these local disturbances of function, on account of which the various alkaloids form veritable elective reagents for the various tissues, are so slight that the functional modification is inappreciable and passes unobserved, the application of the remedy may be continued for months and years unfelt by the living organism. Morphine in therapeutic doses produces stupor and sleep. However, if instead of injecting 1 centigramme, ¼ milligramme be injected, the employment of the remedy may be continued for months, and the subject will not notice it. The same is true of strychnine, and even of the most poisonous alkaloids, such as aconitine, cicutine, etc. Naturally the relation between the degree of toxic action and of tolerable therapeutic dose must be borne in mind.

"The inference is clear and distinct that the mechanism through which the alkaloids can modify all the activities of metamorphosis is fundamentally different from that through which they are modified by medicaments of mineral origin. The action of the latter is primary and incessant, and does not require toxicity in order to achieve wonderful curative results, as may be seen in the employment of iodine, quicksilver, and arsenic.

"The alkaloids, on the other hand, produce in homœopathic doses no appreciable effect, or possess only a transient action in therapeutic doses, or, finally, in toxic doses, they may become dangerous. Under all circumstances, however, they develop a *primarily local* action upon several cell elements, which then becomes general; at the same time metamorphosis undergoes modification when the action upon one or the other nerve or gland function has reached that degree which does *not* longer accord with the normal, harmonious solidarity of all the functions.

"As great as may be the secrecy observed respecting the production of the Koch remedy, it is certain, from the chemical analyses thus far made, that it does not contain metallic salts, and that, in view of its phenomenally toxic action, it must contain a ptomaïne or toxalbumin,—namely, one of those principles formed under the influence of bacteria, which, in recent years, have opened new vistas for pathology.

"In connection with the foregoing, I feel called upon to pay to Robert Koch my tribute of applause, since he has succeeded by dint of systematic and painstaking labor in discovering a new toxic principle, which surpasses in energy all similar substances thus far known. By this discovery he furnishes a new and classic proof of the already great significance of the discovery of ptomaïnes, which serve to illumine the clinical tableau and the character of many acute infectious diseases.

"Permit me here to remind the reader that the great Italian chemist Selmi was the discoverer of ptomaïnes, and that this man reaped only ingratitude for his great scientific achievements, and, as a result of the injustice done him by the government of new-formed Italy, died broken-hearted.

"The discovery of ptomaïnes and toxalbumins, however, has and can have no value from a therapeutic point of view, while to pathology, as before stated, it is of the greatest importance.

"This judgment forces itself imperiously upon me, and when called upon for my opinion, I did not need to see the 'lymph' first, for the published reports respecting its chemical nature were sufficient to impart the scientific certainty that it could not be capable of producing those slow and wonderful curative modifications in the inner organic and biochemical sphere which are indispensable to the correction and cure of the pretuberculous stage,—that is, those organic conditions in consequence of which the patient enters the world burdened with phthisis and lives for years as a consumptive, until finally, as a result of various determining influences, the tuberculous disturbances ensue. Unfortunately, some of those who have had the privilege of seeing the 'lymph' with their own eyes, were intellectually short-sighted; hence the occurrences which have taken place are readily explainable.

"As I have before stated, that form of therapeutic action which is alone capable of successfully treating dyscrasic and dystrophic diseases (provided always that they have not yet entered the anatomical stage of complete incurability) is to be accredited only to exceptional, hygienic, and long-continued influences, or to several medicaments of mineral origin.

"The biological action of the ptomaïnes or toxalbumins can belong only to the category of the biological effects of the alkaloids and the glucosides or other definite organic principles. All these organic substances—among which I include all the chemical vaccines (*matières vaccinates*) discovered of late years—are excreted with more or less rapidity (as we are taught by physiology and general anatomy) by the kidney, without leaving a trace behind.

"Writers have not failed to bring forward the hypothesis that these vaccinating substances during their passage through the animal organism have been capable of so modifying its vitality—that is, its nutrition—as to produce a chemical alteration of the bodily secretions or a dynamic modification of the cells, thus making the latter more congenial to phagocytosis, etc. (Bouchard). But enough of this. Such a mode of argumentation, based on the modification of vitality, on phagocytosis, on increased diapedesis of the leucocytes, etc.,—studies of which are now proceeding in the laboratories after a fashion fairly fantastic,—are rather disposed to recall a chapter from the medical romance of a Silvius de la Boe and a Van Helmont than the progress of the experimental medicine of which our age is so proud. That such studies must be zealously continued in the laboratories no one will deny, but to believe that they will ever exercise a substantial influence on the method of treating disease, or prove successful, is simply *naïve*, and those who pose as the banner-bearers of this movement in research cannot *bona fide* defend it, if they would be honest towards science.

"We greatly regret that those who have

been extravagantly enthusiastic on the subject of the Koch remedy did not at once perceive these distinctions based on the laws of true scientific pharmacology and rational therapy. But this ignorance does not surprise me in the least, as the belief seems to prevail that rational therapy is to be studied only in the laboratory, and as pharmacology, moreover, in order to parade its epithet 'experimental,' and accord with the pure experimentalism of pathology, has become an exclusive branch of the laboratory, thus producing only bitter fruit; and this for the reason that it confines itself to the multiplication of its curves, with or without curare, atropine, etc., thinking thus to ascertain the biological effects of medicines without investigating the innermost nature of their action, which must be regarded as the most important part of the pharmacological problem, if it is to be utilized with profit.

"We need only recall the sad history of the antiperiodic and antithermic agents, another splendid gift from the therapy of the laboratory. I was the first to recognize their true value, and declared them to be poisons as early as the year 1882. But the evil had to run its course, and God only knows how many of the sick have fallen victims to this alleged progress. To-day we are arriving at a recognition of the correctness of my early statements.

"I can foresee no effective, salutary progress in experimental pathology, save as the result of the co-operation of chemistry, physiology, and the clinic, and the fact that my views have been received by distinguished men of science with applause fills me with gratification.

"Accordingly, the biological action of the Koch 'lymph' cannot exercise that slow, modifying influence upon metamorphosis which is alone capable of correcting the biochemical deviations from the physiological type. Either the action is *nil* when the 'lymph' is administered in microscopical doses (and by microscopical doses of the Koch 'lymph' we understand, for example, $\frac{1}{10}$ milligramme), or it is toxic when the 'lymph' is injected in quantities of from .001 to .005. I would even say toxic and lethal, for even these small doses have caused death in some cases, due to ignoring the degree of resistant power in the individual.

"It was, therefore, simply foolish to hope that the Koch 'lymph' would remove that special organic peculiarity which forms the so-called predisposition to tuberculosis, or, in other words, those biochemical conditions which render the organism an appropriate soil for the culture of the tubercular bacillus. In order to modify these organic conditions, many months, if not years, of clinical treatment are required,—in accordance with many analogous instances, such, for example, as the cure of constitutional syphilis, especially in ancient cases. Every physician knows that in the latter instances the iodine and quicksilver treatment must be repeated during the course of many years to insure against the disagreeable surprises of this treacherous evil.

"Hence the question suggested itself to me, how can such a slow modification or alteration of the biochemical conditions of the organism, requiring many years for its consummation, be produced by the Koch 'lymph,' if we bear in mind its chemical character and the terribly toxic action which it inevitably develops when the organism is in condition to respond to its effects? This conclusion seemed to me so convincing that I considered it superfluous to enter on the citation of proofs. Moreover, the facts have unfortunately confirmed my suppositions, and I have penned these comments only in my desire to show that on the day when I openly expressed my opinion of the value of Koch's discovery as a cure for tuberculosis, I was then, as ever in my life, guided only by my convictions, based on scientific principles and incontrovertible clinical observations.

"But how can a true clinician even dream that the organic predisposition to phthisis may be modified and cured by means of an organic medicament, whose action either is not to be recognized (homœopathic doses), or else produces a terrible intoxication, which, fortunately, is only transient, like the poisoning from alkaloids when they do not result fatally?

"Even if Koch's statements respecting the elective or specific action of his 'lymph' are to be accepted as established and true, it would have been more worthy of a man of science had he simply stated the bare truth without further commentary. I am of the opinion that such a course would have been far more humane than that of the daily press (for which Dr. Koch is not at all to blame), which had begun to publish fabulous reports and promises of marvellous cures for the unhappy sufferers from tuberculosis. Now, after the lapse of scarcely two months, disappointment and discouragement have set in, and no one ventures to recall the delirium of enthu-

siasm of last November, or to measure the injury wrought by those reports.

"To resume. The Koch remedy is a powerful organic poison, and in such capacity it acts, putting the organism to a severe test without possessing the power to kill the bacillus or influence the organism in such manner that it shall not continue to yield a soil fitted for the culture of the microbes. This is the inexorable, logical conclusion. Hence the question forces itself upon us: On the basis of what experimental results is it to be assumed of the Koch 'lymph' that it is a cure for incipient phthisis?

"The lay world, as also the great majority of physicians, who, for various reasons, are given to a superficial examination of questions, and accept the crude fact without further thought, greeted my critical study with severe reproach. They express surprise when they see the palpable difference between the unfavorable clinical facts (which I had expected) and the preliminary experiments of Koch, which are not to be questioned,—namely, the immunity from bacillary tuberculosis achieved by him with guinea-pigs by means of injection of his 'lymph.' I see no contradiction whatever.

"The results obtained by Koch in his laboratory are not to be doubted, and are worthy of all admiration. Unhappily, the results obtained in the clinics and hospitals are not less true. In the discourse alluded to above I referred to this clearly enough: 'I can understand that Koch's point of view was very alluring, and I willingly recognize his experiments, in which he imparts to the healthy guinea-pig immunity from the tubercular bacillus. Such facts are neither new nor few in number. Science has recorded them for the past ten years, and the names of Pasteur, Chamberland, Charrin, Roux, Salamon, Bouchard, and others are entered in the golden book of biological science. But between the sincere admiration with which every physician and savant must greet this triumph of the laboratory, on the one hand, and the assumption, on the other, that here are to be sought the means for imparting immunity to a consumptive family, or for the cure of tuberculosis already active, there yawns a chasm, which it is folly to hope to bridge by the resources of the laboratory.

"We shall accordingly find ourselves still confronted by the same lack of experimental consistency, if it be insisted on applying to the human organism the results of laboratory experiments, as though there existed no difference. Here we have the Gordian knot of the whole question. It is so true that we need only express it, in order to comprehend that the failure of such an application is to be confidently anticipated. For what concordance, or identity of biological factors, is to be dreamed of as existing between the healthy guinea-pig, in which tuberculosis has been artificially produced, and into the body of which the protective 'lymph' is injected simultaneously or shortly before or shortly after, and the peculiar and only vaguely-known biological conditions which give rise to a predisposition to tuberculosis? These are two altogether different chemico-biological elements. One need be neither "a prophet nor the son of a prophet" to comprehend and anticipate that one of the two experiments must fail. Now, as it must be allowed that the experiment with the guinea-pig has succeeded, it is not less certain that the trial with a human being must be disappointing. And here lies the great secret.

"Countless experiments have been made of recent years in the laboratories, in order to render various animal species immune from or refractory to certain diseases, by vaccination with chemical substances representing the metabolismic products of the bacteria. I cannot here treat the subject in greater detail; suffice it to say, that from the experiments themselves may be seen how the effects differ, however little the conditions of their existence may vary. How, therefore, can one presume to pass to the clinic with the results of laboratory research, in the *naïve* thought of achieving the same results under very different biochemical conditions, which, moreover, cannot possibly be determined? Is not such an expectation visionary?

"This and no other is the cause of the therapeutic barrenness of so many costly experiments with special reference to those substances from which curative powers were expected, and which are capable of producing deviations from and disturbances of metamorphosis. Unhappily, I have never yet been disappointed by this form of progress, and for a quarter of a century I have been repeating the truth in my lectures and writings. I, therefore, regard as excluded from possibility not only any curative action of the Koch 'lymph' in the treatment of certain organic conditions leading to phthisis, but hold that a discovery proceeding from

the same source and accomplishing the same purpose can never be made, and I shall continue to maintain what I stated at the outset, —'False premises, false consequences.'

"This is the basis of my therapeutic confession of faith. I hope to be pardoned for my outspoken frankness and, what may seem to many, my presumption. My heart fairly fails me when, in the very face of the failure and cruel disappointment which we have been witnessing for years, the interested devotees of a false method in therapeutics, in order to hold themselves harmless from the assaults of truth, delude the credulous public with new hopes clad in stilted phrases, and bombastically glorify the 'new-opened vista,' the 'great future,' the 'certain triumph,' etc.

"Though I have endeavored to show in the foregoing that injections of the Koch 'lymph' are worthless for the cure of tuberculosis of the lungs (since it can neither exterminate the supposititious provocation of the disease or affect the peculiar conditions of the organism), I would, nevertheless, approve of such therapeutic measures if the agent to be injected were harmless in character and availed itself of the courses of the blood only in order to reach the morbid tissue, destroying it by elective action without otherwise assailing the organism. I cannot, however, concede that, in the hope (and even in the certainty) of extinguishing a consequence of disease, while the action of the general cause remains unaffected, and in view of the fact that the bacillus is not destroyed, we are justified in evoking such a disturbance in the entire organism that we thus occasion a new and severely acute form of disease, which, though of short duration, is not unattended with danger. I shall refer only to the very grave phenomena ensuing with many patients after the injection of the Koch remedy, and recall the condition of the heart after the administration of even small doses: Accelerated, dicrotic, irregular, and at times thread-like pulse was the result, so that it became necessary to elevate the function of the heart-muscle and the vascular tone by the administration of alcohol and other excitants.

"I leave unnoted the symptoms caused by the swelling of the tissue surrounding the tubercular neoplasm,—a swelling which, in cases of tuberculosis of the lungs and larynx, may so affect the breathing function as to menace seriously the life of the patient.

"From a physician's point of view, I cannot sanction this mode of treatment, as such a therapy is illogical and contradicts the fundamental maxim, '*Ne noceat!*' which must be borne in mind by every physician in the treatment of his patients. The great celebrity of the investigator who has discovered this method, and even the many years of uninterrupted and arduous labor which he has applied to it, does not suffice to remove my objections. In view of his great scientific accomplishments, I must indeed pay the learned gentleman my tribute of recognition and express my sincere applause; as a physician, however, I feel by no means prompted to agree with him.

"I trust to be pardoned for having thus unreservedly expressed my opinion respecting this alleged discovery of a cure for tuberculosis of the lungs, without any regard to persons. *It is my conviction that thus far Koch has discovered a new and terrible poison, but one which is very far from a cure for tuberculosis.* That is the truth. Should it be my pleasure to see a single case of tuberculosis of the lungs positively cured by the Koch 'lymph,' then I shall give my heart-felt applause, and penitently confess the error of my assertions. But, be it noted, cases of real cure,—not fancied cures, such as are daily described at length in the political journals, which constitute themselves in good faith the heralds of such miracles, *ad usum delphini*, and serve only to deceive the public.

"For the honor of my country I wish that all the distinguished physicians and scientists who are really concerned for the true progress of science would follow the example of eminent French, English, and even German physicians, communicating the true result of their observations without prejudice and without reserve; this is, indeed, the first duty of the true physician, for there is nothing baser than an abuse of the credulity of suffering humanity.

"With respect now to the published results in the cure of lupus, I am forced, as a non-surgeon, to maintain an expectant attitude, as I should be an incompetent judge.

"It is to be hoped that the Koch discovery is an excellent and infallible cure for lupus. However, it is to be remembered that this disease is not altogether identical with tuberculosis of the lungs,—I recall, among other things, the varying virulence of the bacilli, as shown by Lindgard,—and that, aside from this difference, surgery has heretofore achieved cicatrization for a period of several months, and even a year, by means of curetting, scarification, and chemical measures.

"Moreover, from the experience thus far acquired, it by no means results that real cures are to be reported, for we learn, even from the surgeons who have employed the remedy, that relapses not seldom occur; and Bergmann, one of the most enthusiastic apostles of the Koch method, received back into his clinic a lupus patient who had been dismissed as cured after treatment with the Koch solution.

"At present, therefore, there is no occasion for enthusiasm. During my clinical experience of thirty-five years it has always been my custom to cherish the greatest reserve towards new remedies, as well as other things. In the cure of disease, the final dropping of the curtain is represented by a stable cure. Scenic effects are not cures in my eyes.

"It now remains for me to say a few words respecting the value of the Koch 'lymph' as a means of diagnosis. I shall be brief.

"In surgical diseases and in pronounced tuberculosis of the lungs, diagnosis is, unfortunately, free from all doubt; and if it were —happily for the patient—dubious, I should not feel prompted to expose my patients to the dangers connected with the injection of the 'lymph,' in order to have the melancholy certainty that I was really dealing with the tuberculosis, especially as in all theoretical probability (which has been fully confirmed by the results of the investigations of Cornil and others) it is certain that the local reactions arising about the latent tubercles are capable of accelerating the appearance of the severe phenomena proceeding from the existing condition of the lungs. In the face of these effects may we ask, Of what use to the patient is the certainty of the existence of tuberculosis? This certainty is, unfortunately, equivalent to a giving up of the patient and a confession of impotence on the part of the clinician.

"I will concede the great value of a diagnostic auxiliary which enables the physician in dubious cases to recognize the presence of a positively curable disease, such as syphilis, for example. When such cases present themselves to the physician, I believe that, instead of tormenting his patient with the use of the Koch remedy, an iodine-quicksilver cure is to be prescribed. This method will remove every doubt in a more decisive manner, since it will really cure the patient if the case is actually one of syphilis.

"I must believe that no clinician would dare, in cases of dubious diagnosis, to forego the iodine-quicksilver treatment, simply because, after injection of the Koch 'lymph,' that reaction ensues which, according to Koch, should occur only in the presence of tuberculous affections. I say 'should occur,' since even the much vaunted diagnostic value of the 'lymph' has been materially shaken by numerous experiments made by reliable observers in cases of *positive tuberculosis, in which no reaction occurred*, as also with *non-tuberculous patients in whom the well known symptoms of reaction were nevertheless exhibited!* What, then, becomes of this diagnostic value? I must confess that the great Berlin bacteriologist would have done much better had he permitted to mature his own observations which form the basis of his communication of the 13th of November last. The dignity of science and the welfare of humanity would have been thus promoted.

"With respect to the diagnosis of deep-seated tuberculosis, such as the mesenteric and the meningeal, it may be readily seen that the 'lymph' can only produce grave effects, and may even accelerate the death of the patient.

"In view of the foregoing, it may well be asked whether the high valuation of the Koch 'lymph' as a diagnostic means was justified. I will not enter upon further detail here, as I wished to see this question of rational clinical therapy treated only from a general point of view, and, whatever may be urged, rational clinical therapy can never be the legitimate child of bacteriology or of the chemistry of the laboratory. In the pursuit of the latter idea, we have thus far, indeed, discovered wonders in the reagent glass and in the experimental animal, only to be greeted later, as a rule, with disappointment in the hospitals and clinics.

"I hope that a similar destiny is not in store for Koch's discovery, and ardently wish that a whole series of further earnest investigations may show to me that we are in the presence of a true and real therapeutic discovery, and that the latter may not have the experience which recently greeted the notorious antirabic method, to which not a few persons were sacrificed, while the number of cures remain *nil.*

"Germany may continue to chant its hymns of rejoicing, after the fashion of France, which, at an earlier date, could scarcely contain itself with enthusiasm. For the nations mentioned a zone of moderation might be maintained, and this might have been of as much service with respect to Pasteur as it is to-day with regard to Koch."

THE VALUE OF KOCH'S REMEDY IN THE TREATMENT OF LUPUS.

In a series of interesting lectures on the nature of lupus, delivered by MR. JONATHAN HUTCHINSON in the London post-graduate course, the following statements were made as representing his estimate of the value of Koch's remedy in the treatment of lupus (*Lancet*, January 31, 1891).

"As all are aware, it is now about three months since this remarkable fluid—a glycerin solution of substances resulting from the pure cultivation of the tubercle bacillus—was placed in the hands of the profession. It was reputed to have the power, when used by means of hypodermic injection in most minute quantities, of causing the cell-structures adjacent to bacillary deposits to inflame. Very soon after its introduction it was announced that the most remarkable demonstrations of its effects were to be obtained in cases of lupus vulgaris. In these it caused the patches to inflame, and certain small fragments to undergo necrosis, and after this a process of healing set in, which left the patient, if not absolutely cured, at any rate in a greatly improved condition. During the last three months trials of this remedy have been very extensively made, and I now purpose to attempt some sort of brief *résumé* of their results. I know that it will be said that it is too early to arrive at any conclusions, and, in a certain sense, this must be admitted. Very definite results have, however, on some important points been obtained, and it is highly desirable that, for the guidance of future investigators, these should be stated. My own personal experience—that is, as regards patients under my own care—has been very small, but through the kindness of many friends I have had opportunities of collecting facts over a tolerably wide field. In endeavoring to report upon them it may, I think, be stated, in the first place, that the original statement that the injection of Koch's fluid does cause lupus patches to inflame has been well borne out, but not without some striking exceptions. In a case under my own care, the portraits of which I have shown you, and concerning which the diagnosis of lupus vulgaris cannot come into any question, no effect whatever was produced on the patches, although the patient's temperature rose on every occasion after nine or ten successive injections. In this case Dr. Heron made the injections and examined the patient at all stages with the utmost care. I avail myself of his skill as a diagnostician in reference to diseases of the lungs to assure you that the patient had no indications of pulmonary tuberculosis which would explain the recurrence of febrile reaction. After about a month's treatment, the injections having ceased to produce fever, we laid them aside, and the patient is now exactly as he was before they were begun. I have received information concerning more than one case in which somewhat similar results were observed. In one, about which Dr. Abraham is my informant, neither febrile reaction nor local reaction resulted, although the patient displayed nodules of the apple-jelly deposit of lupus in considerable abundance. Without an exception all my friends report that, in the cases in which the lupus patch has been made to inflame, the results, as regards its subsequent improvement, have been very definitely good. Large areas, which had been previously swollen and covered with scab and crust, have been made to heal, and the resulting scar has been flat and sound. No one, however, ventures to report an instance of complete cure. Of the cases which have been shown to me as the most satisfactory, I am bound to say that in every one there has been evidence at some part of the edge of the remains of lupus tissue, ready, I do not doubt, to start into fresh growth on the slightest provocation. In reference to this point I have to make a most important assertion, and that is, that the treatment does not always influence the essential element of lupus. The brown apple jelly-like deposit, which is universally acknowledged as the most characteristic of the lupus conditions, sometimes remains untouched. This assertion is illustrated by a case which Dr. Heron was kind enough to show me, and in which he had practised injections some ten or twelve times. In this instance the inflammatory swelling of the parts affected had been quite got rid of and the patient considered herself very much benefited. Nodules of lupus were, however, scattered about her cheeks in a conspicuous manner, and had she come under my care without my knowing anything of the previous treatment, I should certainly have regarded her as an ordinary case of lupus, still standing in need of efficient treatment by either the cautery or spoon. In the case which Dr. Gayton was kind enough to send us last week—and which had been under Mr. Watson Cheyne's treatment in King's College Hospital, and had received great benefit—you had equal opportunities with myself of judging whether it could be called a cure. The lupus edge was still there. As substan-

tiating my statement that the treatment does not always destroy the most characteristic part of the lupus formation, I might quote from a letter from Mr. Warren Tay, of the London Hospital, who, speaking of a case in which great benefit has been obtained, remarks 'that there still remain nodules which I should much like to attack with the scoop.' The cases which appear to derive the greatest benefit are those in which there is most of inflammatory swelling, and in which the more specialized elements of the lupus process are least abundant. You will see the bearing of this statement. Should it be supported by future facts, we shall be obliged to suspect that the remedy is, after all, one for certain conditions of the inflammatory process, and not for tuberculosis. Even in this position, however, it is possible that it may still prove of great help to us in the treatment of certain forms of lupus. I am not aware that it has yet been tried in any of the cases of what has been described as perfectly quiet lupus, such, for instance, as those of which I showed two portraits illustrating single-patch lupus occurring on the cheeks of healthy persons, characterized by a thick growth of apple-jelly, and by the entire absence of any surrounding inflammation. These cases would be very suitable ones in which to test the power of the fluid in attacking the lupus growth itself; and from what I have seen thus far I quite expect that they would escape its influence. In the more rare forms of lupus the remedy has not yet been tried. On lupus erythematosus, however, a good many experiments have been made. It was foretold by those who believe that what they call 'true' lupus is bacillary, and that lupus erythematosus is not so, that the fluid would have no effect on the latter; and, in the main, this prognostication has been fulfilled. In a very marked case under my own care, and in which Dr. Heron was kind enough to carry out the treatment, the patient had good febrile reactions after repeated injections, but without any inflammation of her lupus patches. This remarkable result was perhaps explained by the supposition that the lady had tuberculosis of the lungs as well. She was, as is usual in lupus erythematosus, of a phthisical family, and she had herself been treated for suspicious symptoms. In her case, a week after we had abandoned the injections in the belief that they were doing no good, the erythematous patches on her face suddenly disappeared almost wholly. A number of disks on the upper part of her chest, however, some of which were so thick and definite that some observers were inclined to regard them as lupus vulgaris, remained wholly untouched. She had had nine or ten injections, and latterly in full doses. I have seen this patient today, and her face patches are already returning to their first condition.

"Apart from the question of its direct influence on the lupus itself, some collateral observations of much interest have been made as to the possible results from Koch's fluid. I am told that it has repeatedly caused general erythematous eruptions on the skin, and, in some, nodular effusions into the cellular tissue. In one case the inflammation of the lupus (on the face) passed into unquestionable erysipelas of a rather severe type, and the patient was for some time in danger. In two cases, at least, during the febrile reaction old chilblains became again inflamed.

"If we are obliged to report that nothing that can be called a cure of lupus has yet been obtained in London practice, it may seem unnecessary to ask whether cures are lasting. On this point, too, however, I am sorry to say that some evidence is already forthcoming. I fear it is the fact that relapses occur very quickly. The patient, who was taken to Berlin by Mr. Malcolm Morris and Dr. Pringle, and was for a time supposed to be almost cured, is now, I am assured by both the gentlemen concerned, in a condition almost as bad as before the treatment.

"If, on the whole, we are obliged to return a qualified verdict as regards this method of treatment in London, it by no means follows that it may not in the future be put to some use. On the contrary, it has in many cases done very great good, and no one can doubt that the fluid possesses very remarkable powers. It may be that in the future we shall learn to combine the older methods of destruction of the lupus deposit by means of cautery or caustic, with suppression of the attendant inflammation by injections. What I have seen would certainly lead to the belief that some patients are by the injections brought into a condition much more favorable for surgical treatment than they were before. The ill effects of the treatment on the general health, although obvious and considerable for a time, seem to pass away. No one has reported to me any instance of permanent damage. I may confess that nothing which I have seen leads me to be hopeful that very prolonged periods of treatment will avail more than short ones. If

febrile reaction has ceased to occur, I do not think that there is any further hope that the lupus nodules will be attacked. On this point, however, as well as on many others, we need further experience. Among those to whom I have been most indebted for the facts upon which the preceding statements are based are Dr. Heron, Mr. Watson Cheyne, Mr. Warren Tay, Dr. Gayton, Dr. Radcliffe Crocker, Dr. Pringle, Mr. Malcolm Morris, Dr. Colcott Fox, Dr. Abraham, and Mr. James Startin. To these gentlemen you and I are alike indebted for the opportunities they have afforded us for seeing their cases this afternoon. For myself I cannot sufficiently express my sense of the compliment they have paid me in placing their facts at my disposal and giving me leave to make my own criticisms. I hope that I have not been premature in expressing the opinions which I have done. If I have spoken with less enthusiasm of the results of Koch's treatment of lupus than it really deserves, I can only say that it will give me great pleasure in the future to change my opinions."

PERITONITIS IN INFANCY AND CHILDHOOD.

Dr. J. Lewis Smith read a paper before the Section in Pediatrics at the meeting of the New York Academy of Medicine, held November 13, 1890 (*New York Medical Journal*, December 13, 1890).

He said that peritonitis was likely to occur at any age, but the most interesting and fatal form was that which occurred in the newly-born. This form had in times past been quite common in maternity wards and in tenement houses, in degraded and filthy families, who had no knowledge or thought of sanitary requirements. There was no doubt that in the etiology of peritonitis in the newly-born microbes played a most important part. The septic matter no doubt entered the system through the umbilicus, usually from the use of foul dressings, foul water employed in washing, foul fingers of the nurse, or other sources. Umbilical inflammation, with perhaps ulceration and the formation of a phlegmon, might occur, and septic matter be taken up by the umbilical lymphatics or blood-vessels and carried into the system. Peritonitis occurred in infancy and childhood from a variety of causes. It sometimes resulted from extension of inflammation from the abdominal walls or from one of the viscera which was the seat of a tumor or adventitious growth, encroaching upon and irritating the peritoneum. Septic infection occasionally caused peritonitis, when the conditions were favorable for it, in older children as well as in the newly-born. Chronic degenerative disease of the kidneys was also a recognized cause of peritonitis, but less frequently in children than in adults. It was now known that a considerable number of the diseases which were formerly supposed to be due to taking cold were caused by microbes. Perhaps there was too great a tendency at the present time to ignore thermal changes in the atmosphere or exposure to cold as a cause of disease. In ill-nourished and scrofulous children inflammation and cheesy degeneration of the mesenteric glands sometimes gave rise to inflammation in the portion of the peritoneum which covered them. But peritonitis in infancy and childhood more frequently resulted from disease of the hollow organs than from that of the solid viscera. Intussusception, attended by bloody stools, tenesmus, vomiting, abdominal tenderness, and the occurrence of an abdominal tumor, was more common in infancy after the age of six months than in any other period of life. Another not infrequent cause was appendicitis due to the lodgement of a foreign substance in the appendix, or of a concretion, which caused by its presence pressure, inflammation, ulceration, and finally perforation. Children less frequently than adults had ulceration of Peyer's patches in typhoid fever, but it sometimes occurred, ending in perforation or rupture and fatal peritonitis. Peritonitis had been known to follow traumatism of the abdomen. Recently a considerable number of cases had been published, showing the microbic origin of peritonitis in certain instances. Some of the cases were caused by accidental inoculation, and others were due to the inhalation of sewer-gas. Experiments had been made, designed to elucidate the casual relation of microbes to peritonitis. Prince had found that the injection into the abdominal cavity of a small amount of an irritant not containing microbes—such as mineral acid, phenol, and nitrate of silver—caused peritonitis, but it was always serofibrinous, never purulent. Grawitz, in his experiments, had shown that, as a rule, two things were necessary for the causation of purulent peritonitis,—to wit, the introduction into the peritoneal cavity of pus-producing organisms, and an abnormal state of the peritoneum from injury or contagious disease.

Another observer had shown that if the peritoneum was in its normal state it might absorb a considerable amount of septic matter with no serious result, but that if it was injured or the subperitoneal connective tissue was exposed to infection, purulent peritonitis was likely to result. Experiments thus far had not perhaps been very satisfactory in throwing light on the microbic origin of peritonitis, but they seemed to show that purulent peritonitis, as a rule, resulted from the action of microbes, and the microbes known to be pathogenic caused peritonitis when injected into the peritoneal cavity, while the non-pathogenic germs did not produce such a result, even in a lesser degree. Tubercular peritonitis occurred much more frequently in infancy and childhood than in adult life. The symptoms, when peritonitis was due to a pre-existing disease, were, of course, accompanied by the symptoms of that disease, by which it might be rendered more or less obscure. The symptoms might begin in any manner, with gradually increasing tenderness of the abdomen, or abruptly with a chill or rigor. Constant pain increased by movements of the body or by pressure was the distinctive symptom occurring in localized peritonitis at the seat of the inflammation, but in diffuse peritonitis it began at some point and gradually extended over the abdomen. Tenderness on pressure was seldom absent, and the pain intensified by coughing or a full inspiration was in most cases seen in the early stage of the disease. The extension of the inflammation over the intestines produced paralysis of their muscular layer so that they became distended with gas. In cases of great abdominal distention the apex of the heart was carried upward, the liver and spleen were pressed upward and backward, and the distended transverse colon or portions of the duodenum or jejunum might lie in front of them, so that the normal dulness on percussion over these organs was replaced by the tympanitic resonance. The percussion-sound over the effused liquid was, of course, dull. The patient was quiet on account of the pain, lying upon the back or side with the knees flexed to relieve the tension, but the position was not uniform, as the legs might even be found extended. Constipation was usually present in the early stage. Vomiting was a common and painful symptom. The pulse was accelerated, in some cases very frequent as well as very feeble. The countenance was anxious, but the mind was clear, or there might be a mild delirium, the speech being incoherent and rambling. Retention of urine was common. In the pathological anatomy of localized peritonitis the action of the cause, as the name implied, was limited to a portion of the peritoneum. In acute diffuse or general peritonitis the inflammation commonly began at one point, but it rapidly extended over the peritoneum. The relative proportion of the different inflammatory products varied greatly in different cases, and in all not only were serum and fibrin present, but pus-corpuscles could be detected under the microscope. The fibrinous exudation upon the peritoneal surface occurred either in patches or continuously over a considerable part of the visceral peritoneum. It was prone to form a covering of varying thickness over the large and immovable organs. The connective tissue underlying the peritoneum underwent proliferation, producing granulations, which, when coming in contact with opposing surfaces, united, forming adhesions, and these at times involved the intestines and viscera, producing disastrous results. In purulent peritonitis, the pus formed, being heavier than the serum, gravitated to the lowest part of the abdominal cavity. In patients that recovered the serum was the first to be absorbed, and the fibrin and pus-cells underwent fatty degeneration, became granular, liquefied, and were absorbed. Sometimes collections of pus became encapsulated and remained inert. By careful attention to the distinctive symptoms a mistake in diagnosis ought not to occur. Peritonitis in children was always a grave disease; in most instances its progress was rapid towards a fatal termination. The author was confident that much could be done in the way of prophylaxis in these cases if a little more attention was given to the matter. Scarcely any disease more urgently required early and judicious treatment than the one under consideration. Proper selection of the diet was a matter of the greatest importance. Such food should be recommended as was most concentrated, predigested, or easy of digestion, and such as would give the minimum amount of fæcal matter. Sterilized milk was by far the best food for this purpose. For children over two years of age some farinaceous food could be added. Purgatives should be avoided. A nutritive or laxative enema was the best for this purpose. Of the drugs, opium, camphor, digitalis, alcohol, and strophanthus were used, as the urgencies of individual cases required. The removal of the cause of a disease, if it

could be effected safely without material injury to the patient, evidently contributed greatly to recovery.

The CHAIRMAN said that a great deal of stress had been laid from time to time upon the grape-seed point. He had never yet found such seeds in any appendix vermiformis. He thought it was a little hard on children that, on the strength of this apprehension, they were to be debarred from eating fruit.

DR. J. E. WINTERS thought that the most important causes of peritonitis in children were typhlitis, perityphlitis, appendicitis, traumatism, tuberculous disease, and intussusception. In regard to the first three conditions, the cases, of course, required to be seen early, when he thought that a critical examination ought to result in a correct diagnosis. The traumatic cases were more difficult, for the reason that most children were unwilling to acknowledge the indiscretion which had led up to the traumatism. In dispensary practice this was particularly difficult to elicit; but brutal treatment by the parents was a frequent cause of the peritonitis. The tubercular variety required acquaintance with the family history, and called for a thorough examination as to the existence of general tubercular disease in the patient. Without all these points, few physicians would be willing to make a diagnosis of tubercular disease in the peritoneal cavity. In intussusception the symptoms were sufficiently pronounced to make a diagnosis tolerably easy. A diagnosis of peritonitis from either of the three first-named causes having been made, then came the question of management. He thought that at the present time most men used cold. The inflammatory processes were sufficiently superficial to be influenced by the external application of cold, and he thought that the results were, on the whole, more favorable than from heat. Only in the case of absolute inability on the part of the patient to tolerate its application would he use anything for external application except ice. If cold would not relieve the pain, then morphine must be used. It was important to remove all substances from the large intestines, and for this purpose he thought that it was best to employ small doses of triturated calomel.

The frequent injection of ice-cold water into the rectum was desirable after the use of the calomel, or of castor oil. In the traumatic cases, having gained the confidence of the child and obtained a careful history of the case, he thought that cold applications and a clearing out of the alimentary canal were, as a rule, sufficient, together with the strictest dietetic management. In the tuberculous cases the physician could endeavor to give relief by counter-irritation by means of iodine. In this way the early indications might be met. If suppuration was excepted, an operation might be resorted to. In cases of perityphlitis and appendicitis, where, having made a casual diagnosis, and having failed by judicious means to relieve the local symptoms, laparotomy should be suggested. As now undertaken, the operation was not serious, and it was far simpler at the outset than after extensive adhesions and infiltrations had taken place.

DR. SMITH thought that, if the surgeons were to examine the concretions carefully which they found in the appendices, they would often discover that seeds and other foreign bodies were the real cause of the trouble. He was not inclined to withdraw from the stand he had taken in the matter of grape-seeds.

TREATMENT OF DIABETIC COMA.

In the *Berliner Klinische Wochenschrift* for August 25, 1890, DR. SCHMITZ publishes his views as to the nature and causes of diabetic coma and his treatment of it. This paper has been analyzed by DR. W. A. STEWART, who publishes an abtract of it in the *Medical Chronicle* for November, 1890.

The author recognizes two distinct causes. The first is weakness of the heart's action, caused by the action of the sugar in the blood on the muscular fibres of the heart. In diabetic subjects, even when fat and seemingly in good condition, the body muscles are lax and soft, and the results are insecure gait and weariness easily produced. The heart muscle, he argues (and post-mortems support him), is in a similar condition,—also suffering from degeneration of its fibres. The cyanotic face, the quick breathing, and the slow, small pulse, getting quick and irregular with the slightest exertion, point in that direction. Then the cardiac impulse is hardly perceptible, the area of heart's dulness is increased in breadth, and, on auscultation, not only at the apex, but on the aorta, the first sound is anything but clear. In severe cases it is barely audible, or even inaudible, and the beat, especially on exertion, is frequently irregular. With such a heart there goes short breath,

giddiness, sounding in the ears, and great sense of weakness. Suppose such a heart is wearied out by over-exertion, the result is that the breathing is affected, the appetite disappears, the head suffers from pain, giddiness, and an inclination to vomit, and if no precautions are taken, or prove of no avail, the arteries get more and more empty, the veins more and more full, and carbonic acid accumulates in the blood, somnolence steals on, coma succeeds, and the patient dies poisoned. Instead of striking work gradually, the heart may stop suddenly, and in some cases unexpectedly burst without even any preliminary over-exertion or over-exhaustion (*e.g.*, case of Baron von Haymerle, eight years ago).

In such cases the line of treatment is plain. Anything exciting the heart, medicinal or other, must be avoided. Hill climbing, stair climbing, long walks, early rising, Venus and Bacchus in excess, are all to be avoided, as also are bromide of potassium, all combinations of potassium, salicyl, antipyrin, antifebrin, and hot baths. Also narcotics, except when absolutely necessary, and then carefully used. Nutritious, but easily-digested food, a moderate amount of alcohol, fresh and invigorating air,—these are the best drugs. Of course, one must not lose sight of the ordinary diabetic treatment ; the above refers to cardiac failure.

In a pressing case the patient is to be kept in the recumbent position, and must neither stand up nor sit up, even for stools or urinating. Stimulants by the mouth, or, preferably, if apt to cause vomiting, subcutaneously (*e.g.*, musk and camphor). The best stimulant of all is black coffee. With alcohol in large doses it is necessary to be careful on account of the succeeding depression favoring collapse. The neglected *castoreum sibiricum*, not *canadense*, he considers a very good stimulant. The great danger lies in letting the patients up too soon, and the great difficulty is keeping them in bed long enough. Schmitz makes it a rule not to let his patients get up until the first sound of the heart, indistinct or vanished, again becomes clear. He gives five interesting cases illustrating well his theory and treatment.

So far as regards the first. The second form of diabetic coma he describes as an acute self-poisoning, which has been named, although not rightly, acetonæmia. This condition is preceded by symptoms mistaken for indigestion, or slight gastric catarrh,—*e.g.*, lack of appetite coming on suddenly, eructations, especially in the morning, of foul gases, great sleepiness and weariness. The sleep, like that of drunkenness, leaves the patient more weary, feeble, and heavy-headed than before it. There is usually constipation, sometimes diarrhœa ; the tongue is dry and coated, and the breath smells badly. This condition lasts for about two days, and then the patient gets restless, groans and laments in his sleepy state. The respirations increase to 45, the pulse to 130 or more. The temperature is always raised (38°, 39°, and over). He requires a loud call to rouse him, seems peevish, hardly answers a question, and again relapses into his sleepy condition. He complains, when asked, of thirst and of pains in the upper left side of the abdomen, which, however, is not painful on pressure. These pains or colic attacks come on from time to time, and must be very acute, as they awaken the patient and cause him to cry out aloud. After violent efforts he vomits some green-colored fluid, and then the maddening pain seems to abate somewhat, and he falls asleep until another attack.

A physical examination of the *heart and lungs reveals nothing abnormal.* The pupils are mostly contracted, and react but slightly. Towards the end violent clonic and tonic spasms set in, and death follows in deep coma. It comes quickly, often in ten hours.

The colic, the high temperature, and the clear heart-sounds distinguish this form of coma from that produced by cardiac failure. The treatment is beautifully simple. It consists in clearing out the bowels, constipated or not, with 1 to 2 tablespoonfuls of castor oil. "The poison, be it ptomaïne or toxin, or whatever else, is a product of decomposition in the bowel." The case is simply one of poison ; the poison lies in the bowel, and the indications accordingly are to get rid of it as soon as possible. After a thorough purging, resulting in a profusion of black, foul, putrid stools, recovery is remarkably quick. Even in diarrhœa he gives castor oil, and the result is equally good. The purging does not weaken the patient, who seems better after than before the attack. Of eight cases, all equally bad, four not treated with the oil died, and four treated with it speedily recovered. One of these cases may serve as a sample :

"D., three years diabetic, and once in Neuenahr before, fell ill on the journey, and summoned me by telegraph to Cologne. The patient had already suffered some days from constipation, had had eructations of putrid gas, and was suddenly seized with the most violent pains and vomiting. I found the pa-

tient in a very somnolent condition, scarcely able to answer questions. Temperature, 38.6° ; pulse, 130 ; respiration, 40. Here also I did not delay, but gave at once a tablespoonful and a half of castor oil, and the same dose an hour after. After an hour and a half the pains and sleepiness departed, and, when, after two hours, he was relieved of great masses of abominably stinking fæces, his condition became rapidly and remarkably better. He got up the following day, and continued his journey on the same day to Neuenahr, where he continued to improve. He remembered for a long time the abominable taste of the gas."

The poison is in the fæces ; who will isolate it?

BASSORIN PASTE—A NEW BASE FOR DERMATOLOGICAL PREPARATIONS.

In the *Journal of Cutaneous and Genito-Urinary Diseases* for February, 1891, Dr. George T. Elliot describes a preparation as a base for dermatological preparations belonging to the class of vegetable mucilages derived from bassora, — gum tragacanth. This substance, which was prepared under his direction by Mr. Lascar, the pharmacist of the Demilt Dispensary, is tasteless, odorless, and almost colorless, insoluble in cold water, and swelling up into a viscous mass when treated with hot water. On being heated with aqueous solutions of alkalies, it is converted into a gum, soluble in water, and, by treating with sulphuric acid, it is transformed into a non-fermentable sugar. This substance—bassorin—is mixed with water, glycerin, and dextrin, and a compound is obtained to which the name bassorin paste can be given. When composed of the substances mentioned, bassorin paste is of the consistency of a jelly, tawny in color, resembling somewhat vaseline. It has no particular odor, is absolutely neutral in reaction, does not decompose when kept a length of time. When exposed to the air it becomes dried, and hence bassorin paste should be kept in well-closed jars ; but, even when it has hardened, rubbing it up again with a little water makes it as good as at first. The base is claimed not to come off when once dried on the skin, and thus soiling of the linen or bed-clothes is avoided. When it is desired to remove it, this can be accomplished at any time by a little water or a damp sponge or absorbent cotton Almost any drug at will may be incorporated with the bassorin base. If the one used be soluble in water contained in the paste, the color of the latter is unchanged ; but, if insoluble, then the color will vary, according to that of the substance added to it. Those drugs which exist only as fluids cannot be mixed, however, with the base, and neither can alcoholic solutions ; but fats may be, yet to a limited extent. The former are excluded, for the reason that they render the base too liquid, and the alcohols cause it to become brittle and hard. The proportion of the fats must be small, for the reason that, if large, they would impair the property the paste has of drying and adhering to the skin. All substances, however, which exist in a solid form are easily incorporated with it in proportions as large as are ever used or found necessary. For instance, zinc oxide may be mixed with the base to the extent of thirty or more per cent. ; carbonate of magnesium, ten or more ; chrysarobin, fifteen or more ; salicylic acid, salicylate of sodium, iodoform, resorcin, boric acid, borate of sodium, sulphur, etc., each and all, incorporate perfectly with the bassorin paste, and without changing its nature or its properties. So, also, while the percentages of the tars do not go quite as high, on account of their oily nature, they may usually be incorporated to the strength generally deemed necessary, though then it is advisable to add ten per cent. of zinc oxide or some neutral powder, as chalk, to counteract any possible impairment of the base's characteristics.

Dr. Elliot does not publish the precise details of the manufacture of this base, but promises that Mr. Lascar will shortly do so, and publish in the columns of one of the pharmaceutical journals, when we will lay the details before our readers.

Dr. Elliot, in conclusion, summarizes the advantages of this bassorin paste over other excipients, as follows :

1. Bassorin paste is a perfectly neutral substance, which, of itself, produces no irritation whatever, and when used alone it acts simply as a protective to the skin. It does not become rancid or decompose, or undergo change when kept for a length of time, unless it be exposed in an open vessel. When this is done it becomes dry and hard, but even then rubbing it up with a little water renders it again as serviceable as at first.

2. It is easy and simple in application, requiring only to be spread upon the skin with the finger or a brush. It dries in the space of a few minutes if so applied, adheres closely,

does not rub off and soil the linen, but forms a flexible coat, which does not interfere with the movements of the body. When its removal is desired, the preparation can be washed off with a little water or a damp cloth or sponge. It remains *in situ* without change for a variable length of time, depending upon the condition of the surface on which it has been applied.

3. With the bassorin paste almost any drug can be incorporated; those which exist in the form of powders or in solid forms in any amount desired; the tars, ichthyol, and oily substances in smaller percentages, but sufficient for all practical purposes.

4. The action of drugs incorporated with it and their effect upon disease appears to be as good as when such are used in other excipients, or perhaps better in some cases.

5. It is of wide applicability, and of value in both acute and chronic forms of disease, its use being limited only by the degree of moisture on the surface being treated or to which it may be exposed.

These properties possessed by the bassorin paste render it, as may be seen, superior to ointments, for the reasons, among others, that it is difficult to keep the latter in constant contact with the diseased surface; that salves soil and stain the linen, and offer such other objectionable features as greasiness, risk of becoming rancid, etc., to say nothing of the discomfort entailed upon the patients using them. It is also of wider application than the collodions and traumaticins, owing to the irritation of the ether and chloroform contained in them, their contractile property, the limited extent of surface over which they can be applied, and the difficulty experienced in removing them when desired.

The bassorin paste would seem to be also superior to the gelatin preparations, in that these latter are more or less cumbersome in their application, having to be heated freshly whenever used, entailing a waste of time, and also frequent and practically unnecessary visits by the patient. Drugs incorporated with the gelatins have also seemed to me not to act as favorably upon disease as when mixed with the bassorin base.

TREATMENT OF ERYSIPELAS.

An elaborate research, clinical and bacteriological, has recently been published by Professor Nussbaum's assistant, Dr. Julius Fessler, on the treatment of erysipelas by ichthyol, a plan which has been for some years extensively adopted in Munich. From laboratory experiments it was evident that, though ichthyol has only a slight effect in preventing the development of staphylococci, it has a very potent deterrent influence on the multiplication of streptococci, and it is well known that it is the latter kind of bacteria that are the cause of erysipelas. The method of treatment consists mainly of rubbing a strong ichthyol ointment energetically, and for ten minutes at a time, into the affected surface and its neighborhood; ichthyol in the form of pills may also be given internally. Where there is a wound it must be very carefully disinfected, and an antiseptic dressing applied. The results of this treatment, as compared with ordinary methods, are embodied in several instructive tables. From these it appears that, while the mean duration of the cases treated by other methods from 1880 to 1888 was about twelve days, in no single year falling below nine days, the cases treated by ichthyol from 1886 to 1888 presented a mean duration of under seven days, while in the first half of 1889 it fell to 5.6 days.—*Lancet*, January 10, 1891.

THE MEDICAL ASPECTS OF TREPHINING IN EPILEPSY.

Dr. J. C. Minor read a paper before the Section of Theory and Practice of Medicine of the New York Academy of Medicine, at the meeting held November 18, 1890 (*New York Medical Journal*, December 13, 1890).

He said that, from long clinical observation, he had concluded that epilepsy did not disappear spontaneously, but that about one-half of all the cases presented for treatment were curable, whether the cases called for medical or for surgical treatment. The reason that surgical interference did not offer better results was, the speaker thought, due to the cases not having been properly selected. He thought that the indications for trephining in epilepsy were pretty definitely marked out. The indications were described under three headings: 1. Those that were plainly traumatic and presented a depressed fracture of the skull, osteitis, and tumors of the brain. 2. Those without any apparent lesion of the skull, but with old cicatrices of the scalp. 3. All those cases of epilepsy the symptoms of which indicated cortical lesions. The speaker was satisfied that more than half

the cases presenting for treatment would come under one of the above groups. The history of a case was then reported. The patient, a young man, 17 years of age, had five years ago been hit on the head with a brick which had fallen from quite a height, producing only a scalp-wound. Four years later the first attack came on, and during the last year epilepsy had become fully established. The attacks came on with a distinct aura, contractions commencing in the right hand and arm. Pressure on the scar would bring on the aura and produce a typical attack. Trephining in this case had disclosed no injury to the skull, but the removal of the cicatrix had ameliorated the condition. The speaker, from his observations in this case, was led to the conclusion that it was always well to begin the treatment, in cases presenting cicatrices, by removing the scar. Several cases had been reported cured, treated in this manner, and he thought it was well worth trial. He did not think that in trephining at the site of injury the actual lesion caused by it could be found in every case. The contraindications for operative interference were in all those cases where the cause was not clearly defined and in those of long standing where the patient's mind had become enfeebled and the general condition would offer no hope of recovery. Finally, when the indications were for surgical treatment, the operation should be done promptly, as by so doing the best possible chance would be given to the patient.

In the discussion which followed—

Dr. Robert F. Weir was quite in accord with the rules laid down by the speaker. Despite the fact that operations were being done on the brain by some of the most careful surgeons, the mortality was still quite high, averaging from fifteen to twenty per cent. His experience in brain surgery had led to the conclusion that much would yet be done in this direction, but that when the technique of the operation was better understood the results would be better.

Dr. Robert Abbe reported the histories of two cases in which an operation had been performed, the results of which led to the conclusion that conservatism was to be practised in operating in such cases.

Dr. E. D. Fisher thought that it was a difficult matter to say which cases should be operated on and which not. He thought that chronic epilepsy, traumatic lesions with consequent organic lesion, congenital spastic paraplegias with associated epilepsy, and a focal lesion becoming general were certainly not suitable for operation. Cases had been met with where the scar was a source of irritation, but, again, it was often present when it did cause any trouble whatever, so he could not agree with the speaker in thinking that it was a good thing to trephine in these cases. He had a case which had appeared to offer every indication for trephining. The operation had seemed to be a success, the patient had improved for two or three weeks, but had after that relapsed into his old condition. It was the speaker's opinion that all the cases of idiopathic type of epilepsy were originally traumatic.

Dr. L. C. Gray thought that, in reviewing the question of the indication for operation in epilepsy, it would be just as well to first ask what was epilepsy. It was still a question as to whether epilepsy was a disease or a symptom of one, and if either, what were the cause and nature of it? Whether it might not be due to peripheral irritation had been pretty thoroughly gone into, and it was found that after every source of irritation had been removed the attacks went on the same as before. The histories and data were wanting in definite value. This was thought to be due to the fact that cases were not kept under observation long enough, and not followed up with a definite object. Idiopathic epilepsy with marked changes had been known to go on for years without a fit having occurred. There was no doubt that many of the cases were organic in origin. Those that were due to meningitis in early infancy certainly could not be operated upon. Such cases as were due to the same causes were called in the adult idiopathic, simply because the definite course of the disease was not known. The traumatic cases offered but little better results for operative interference on account of the very limited knowledge of the focal centres. The only ones isolated were those of the arm, leg, speech, word-deafness, and hæmianopsia; when we undertook to go beyond that point we were in the field of speculation. It was still a question whether, if operation were performed in cortical epilepsy, the habit of the explosion was not too confirmed to cease. The speaker related the history of a case of subcortical lesion in which no loss of consciousness had occurred. He thought the whole question bearing on epilepsy was still distinctly *sub judice*.

Dr. Minor said that the indications and rules laid down by him had been made up principally from reports and his own clinical experience. He was sure that some cases

had been cured of the attacks by the operation, but he was also of the opinion, as Dr. Gray had expressed it, that the habit could not be easily broken up and that it was likely to return. In operating in cases of idiopathic epilepsy where no scar could be found he had never known it to do the patients harm. The operation in these cases was done on the principle of cerebral pressure. He had recently seen an old patient upon whom he had operated some twenty years ago, removing a large portion of the frontal bone with a quantity of brain tissue. It was interesting to know that there had never been any development of epilepsy, but the mental and moral degradation was complete.

ALBUMINURIA IN PREGNANCY.

EHRHARDT and FAVRE (*Nouvelles Archives d'Obstét. et de Gynéc.*, September, 1890) discuss this subject in relation to a mild attack of puerperal diphtheria in the Paris Maternité. They sum up past theories which have influenced treatment. Rayer traced the albuminuria to hydræmia, which exists during pregnancy. He noted that injection of water into the veins of an animal caused albuminuria, but this fact does not prove his theory. Claude Bernard traced albuminuria to a state of superalbuminosis in pregnancy. Injections of white of egg into the circulation caused albumen to appear in the urine. Gothwald and Monas held that the phenomenon was caused by increased blood-pressure, the gravid uterus compressing the aorta below the renal arteries. Others believed that the uterus, by pressure on the ureters, caused renal disease. Lastly, some pathologists traced the albuminuria to nerve influences carried on by communications between the uterine and the renal plexuses. None of these theories, says Drs. Ehrhardt and Favre, explain why pregnant women suffer from albuminuria only in exceptional cases. They trace the complication to local disease. They examined three hundred placentæ. Of these, twenty were from cases of albuminuria. In nineteen of these placentæ white infarcts were detected, and all the patients except two were subject to severe leucorrhœa when not gravid, and often to colicky pains during menstruation, symptomatic of endometritis. Colonies of bacteria were found in the infarcts, and when some germs taken from infarcts in the placentæ of patients who had suffered from eclampsia as well as albuminuria were injected into the veins of rabbits and guinea-pigs, parenchymatous nephritis was set up. Thus the morbid changes in the decidua which cause placental infarcts are induced by the same agency that induces the nephritis of pregnancy. This agency is the presence of germs in the placenta, which germs produce in non-pregnant patients leucorrhœa and other symptoms of chronic endometritis. The focus of infection being the uterine mucous membrane, that structure requires attention and treatment. When it is unhealthy, the patient may repeatedly bear fœtuses which die before birth through disease of the placenta,—that same disease which, in the opinion of Drs. Ehrhardt and Favre, causes the nephritis of pregnancy, with consequent albuminuria. They intend shortly to describe the precise nature of the disease in the kidneys in these cases. The moral they would draw is,—never neglect uterine discharges.—*British Medical Journal*, January 3, 1891.

PALPATION OF THE NORMAL UTERINE APPENDAGES.

At the December meeting of the Gynæcological and Obstetrical Society of Baltimore, DR. HOWARD A. KELLY read a paper upon the "Palpation of the Normal Uterine Appendages (published in full in the February number of the *American Journal of Obstetrics*). He stated that the normal uterine appendages could always be palpated. There are two avenues of approach,—by the vagina and by the rectum,—and three ways of utilizing these avenues,—first, with one hand; secondly, with two hands, employed bimanually, either by vagina or rectum; and, thirdly, the trimanual method,—by vagina and by rectum.

First.—The examination with one hand is unsatisfactory, and the ovary cannot even be felt unless abnormally displaced downward into the recto-uterine pouch.

Secondly.—The success of the bimanual examination depends upon the downward pressure, with the external hand displacing the abdominal walls in the direction of the ovary to be palpated, and thus affording a resistant plane, against which the ovary can be felt by the internal hand. The internal hand must be used to invaginate the perineum, which is thus displaced upward into the pelvis. This invagination gives the examining-finger, even though it be a short one, the necessary length. One, often even

two inches are thus gained to the palpating-finger. Care must be taken in making the pressure necessary to produce this invagination, not to stiffen all the muscles of the forearm, thus impairing the tactile sense.

The rectum is, of all others, the best avenue for approaching the structures lateral to the uterus, affording, as it does, a wide, open channel throughout the whole length of the pelvis.

Where the structures cannot be reached at once through the rectum, they are brought within easy touch by bringing the uterus and ovaries into an *artificial retroposed* anteflexion, the mechanism of which was carefully described by diagrams.

Dr. Kelly had in this way palpated fibroid tumors on the posterior surface of the uterus near the fundus not as large as a pea.

Thirdly.—The trimanual examination is conducted either by the vagina, or by the rectum and vagina, assisted with the hand above. The peculiarity of this method is an *artificial descensus uteri.* The uterus is grasped with a pair of bullet forceps, and drawn downward until the cervix is seen at the vaginal outlet, and, while an assistant holds it in this position, the gynæcologist uses his hands bimanually. To obviate the employment of an assistant, Dr. Kelly has invented an instrument which he calls the corrugated tenaculum, flattened and roughened so that it can be readily held between the last phalanges of the third and fourth fingers and the ball of the thumb, while the index-finger of the same hand, assisted by the abdominal hand above, is engaged in making a vaginal or rectal examination.

By one or the other of these methods, the uterus, broad ligaments, and ovaries and tubes are within reach of a most thorough and searching examination, revealing at once the smallest abnormities.

HABITUAL ABORTION.

At the meeting of the West London Medico-Chirurgical Society, held January 2, 1891, Dr. Leith Napier read a paper on "Habitual Abortion."

Dr. Napier said the term "habitual abortion" being limited to a recurrence of abortion three or more times, then discussed in an exhaustive manner the various methods of treatment, classifying them under four headings,—1, rest or exercise, insisting on the necessity of absolute rest for at least six days in the month; 2, local cure of uterine disease, chronic endometritis being regarded as the chief cause of abortion, in that retroflexion and other displacements, with atony of the mucous membrane, leucorrhœa, etc., were regarded as resulting from chronic uterine inflammations or congestions; 3, constitutional treatment; and, 4, drug treatment. The value of local treatment was strongly urged, and in estimating the comparative utility of drugs, the prolonged exhibition of mercury, even in cases of a non-specific nature, was extolled above all other therapy; while, as a uterine sedative, viburnum was preferred to any other drug by the author of the paper, in whose practice seventy-seven per cent. of habitual aborters had borne living children after treatment by local methods and drugs.

A discussion ensued, in which Dr. Handfield Jones thought that too great stress had been laid by Dr. Napier on local treatment. He regarded heart-disease as the primary cause of chronic uterine disease and retroflexion, and pointed out that the commonest epoch for abortion was that at which the gravid uterus was striving to rise out of the pelvis, cardiac disease generally causing abortion between the fourth and fifth month, failure of the left ventricle leading to uterine stasis, congestion, and petechial hemorrhages. —*Lancet*, January 10, 1891.

COMPARATIVE ABSORBABILITY OF LARD AND VASELINE BY THE SKIN.

There is a gradually growing tendency to substitute vaseline for lard as an excipient in the preparation of various ointments, and the question at once arises as to whether the skin possesses an equal power for absorbing these two fats. This point has been investigated by Drs. Adam and Schoumacher, whose results are published in the *Repertoire de Pharmacie* for January 20, 1891.

Starting with the attempt to determine as to whether these fats are actually absorbed by the skin, and in what degree, they prepared an ointment with lard containing variable quantities of the hydrochlorate of strychnine, applying this ointment without friction to the shaved head of a dog, applications being made at this point so as to prevent the animal absorbing the poison by licking the surface. They further took the precaution to see that there was no solution of continuity in the skin. They found that an

ointment containing ¾ grain of the strychnine salt to 120 grains of lard produced no toxic symptoms. With an ointment containing 7 grains of the strychnine salt and the same quantity of lard they noted simply slight hyperæsthesia, while in an ointment containing 30 grains of the salt (dog weighing ten pounds) tetanic convulsions were produced in about three minutes and death in twenty minutes, while a dog weighing seventy-two pounds died from the same quantity in twelve hours.

On the other hand, when the ointments were prepared with vaseline, even when it contained 30 grains of the strychnine salt, no symptoms of poisoning whatever were produced. The authors then experimented with atropine, and obtained precisely similar results. With an ointment composed of 120 grains of lard and 15 grains of atropine, there was slight mydriasis produced at the end of six hours, in a dog weighing forty-eight pounds, while the action of a similar ointment prepared with vaseline was absolutely negative. The authors conclude from their experiments that the absorption of ointments made with lard actually takes place, even although it is extremely slight in a dog, and it is necessary to employ doses at least a thousand times larger to produce death than is required to produce the same effect when administered subcutaneously, while in the case of vaseline, when the skin is intact, there is absolutely no absorption of ointments in which this fat serves as an excipient.

LUFF (*Brit. Journ. of Derm.*, June, 1890) summarizes the results of his experiments on the absorption of drugs from ointments with the bladders of goats, as follows: With vaseline and iodide of potassium, exosmose commenced at the end of the first hour; with lard and iodide of potassium, at the end of the ninth hour; with lanolin and iodide of potassium, the result was *nil* up to the twenty-fourth hour. With vaseline and carbolic acid, exosmose commenced at the end of two hours and three-quarters; with lard and carbolic acid, at the end of seven hours; with lanolin and carbolic acid, the result was *nil* at the twenty-fourth hour. With vaseline and resorcin, exosmose commenced at the end of the tenth hour; with lard and resorcin, at the end of the fifteenth hour; with lanolin and resorcin, the result was *nil* at the twenty-fourth hour. Luff concludes that if it is desired to obtain the rapid absorption of medicaments in the circulation, it is better to use vaseline, and that for local therapeutic purposes pomades made with vaseline should be preferred. This latter substance causes the incorporated medicaments to keep for a much longer time.—*British Medical Journal*, January 3, 1891.

DIGITALIS AND STRYCHNINE AS CIRCULATORY STIMULANTS.

Digitalis, caffeine, strophanthus, scoparius, and adonis vernalis constitute a most useful group of agents that exhibit an action upon the circulatory apparatus commonly spoken of as tonic or stimulant; but, when the physiological effects of these drugs are considered critically from the stand-point of their application to diseased states, it will be seen that their use is more limited than is generally supposed. The concomitant actions upon parts and functions of the organism, other than the heart and circulation possessed by each, frequently present a barrier to their employment, even where the circulatory symptoms would seem to indicate their prompt administration. The indications for the use of digitalis in heart-affections are clearly understood, but the reasons for and against its use in many cases of a weakened and failing circulation do not appear to be as firmly established. This view of the question, together with strong arguments for the use of strychnine as a circulatory stimulant, form the basis of a valuable paper published by DR. BRADFUTE, (*New York Med. Journ.*, January 10, 1891), who in the first place maintains that in the class of constitutional diseases, especially those characterized by a continuous high temperature, accompanied by any of the various forms of degenerative change in the organs and muscular system, digitalis is not the remedy, and where these changes affect markedly the cardiac structure it is conspicuously contraindicated. The action of the drug upon the muscular fibre is one of stimulation, followed by an increase in its force power, and, if the fibre is surrounded by or contains within its substance granules or particles of fatty change, it can be readily seen that the indications are for the relief of overwork, and not to compel it to do what it is already physically incapacitated to perform. For example, in typhoid fever the condition just outlined is always present, and the administration of digitalis in doses sufficient to produce even a slight physiological effect cannot fail to do harm; but that this fact is frequently overlooked, and by practitioners of eminence, there is ample evidence. In addi-

tion to the ugly action of digitalis upon diseased heart-tissue, its property of contracting the arterioles, causing a rise in the blood-pressure, increases the total amount of cardiac work necessary to be done, which is so injurious as to result sometimes in practically a paralysis of the entire organ,—a mishap that has occurred after a sudden change from the recumbent to the erect posture in instances of undue exhibition of the drug where there was no interference by disease with the normal function of the heart-fibre. Its influence upon the inhibitory centres also offers an obstacle to its use when the above-mentioned objections may not exist, and on account of this it is well to remember that, as a rule, subject to modifications attendant upon exceptional cases, a weak and slow heart is not amenable to the curative effects of digitalis; rather is it a weak and rapid heart that presents the most favorable opportunity for the display of its peculiar action. Phosphorus-poisoning, typhus and yellow fevers, atheroma, and fatty heart are affections presenting a pathological anatomy contraindicating the employment of digitalis, especially in the last stages of these diseases. Aside from its use in simple heart-disease, unless very skilfully handled, digitalis is only effective in the failing circulation of hemorrhage, shock, and certain acute affections, especially when the cardiac movements are very rapid, where the result desired is a bracing up, as it were, of the general circulatory apparatus until nature has time to recover herself. In shock following head injuries, when the heart is slow, nitroglycerin is the better agent, as it paralyzes the inhibitory centres and dilates the arterioles, thus promoting the activity of the heart and increasing the rapidity of the blood-current. But in these instances there are no degenerative changes in the heart-muscle to negative violent stimulation of the fibre. In acute phthisis, accompanied by an irritative fever and a rapid and sometimes tumultuous heart, digitalis is often very useful, but it is manifestly unsafe to administer it in large doses. The Harveian lecturer of 1890 calls attention to the independence of the systemic and pulmonary circulations, which opens up a new field for the study of pulmonary therapeutics; and it may be that future experiments and observations may preclude the employment of many of the drugs now used in lung-affections; but, under our present knowledge, digitalis is an excellent remedy for the failing heart of continued pulmonary hemorrhage and the gray hepatization stage of pneumonia. In the latter, digitalis does good so long as the heart does not beat below the normal rate; when the pulse drops below 70, some other remedy must be given. In the first and second stages of pneumonia, when active inflammation is going on, digitalis is out of place, as it only causes the heart to pump more blood into an already surcharged area, and can have but little influence over the temperature. In myocarditis, where exudative material is poured out in and around the muscular substance, digitalis adds insult to injury, and the interference with function from the disease is only increased.

From these few remarks it can easily be seen that some of the contraindications that may be present in disease prohibiting the use of digitalis, or a remedy having a similar action, are congestion and inflammatory obstruction in the pulmonary structure; degenerative changes in the muscular system, including the heart; general interruption of the nutritive processes, with accumulation of serum in the tissues; sudden cardiac failure; and all conditions in which the heart-beats are less than normal. Of course no iron-clad rules can be laid down; but if the drug is given in maladies characterized by any of the above-mentioned lesions, it must be used with great care.

In selecting a remedy to combat a failing circulation, all the structural changes and diminished or lost functions must be accurately studied and the influences resulting therefrom duly considered. Without the intelligence accruing from such a consideration of a given case, it is impossible to apply a proper drug, no matter how well known is its action. A thorough knowledge of the normal physiological state of the patient, the pathological changes that have taken place, and the physiological action of the drug is essential to successful therapeutics, and in no instance is a familiarity with these three points more important than in a case of failing circulation.

In those protracted diseases in which this formidable symptom arises, the general condition of the patient may be summarized as follows: The muscular system is weak, flabby, degenerated, and ill nourished; the nervous system is reflexly disorganized; the nerve-conducting paths, chiefly at the periphery, are partially or entirely obstructed, so that tissue sensation and motility are interfered with and vaso-motor paresis is marked, thus checking normal physiological change

in part or even in places completely: the secretory structures are either exhausted—not functionating—or their products are unfit for use; the circulatory apparatus is devoid of tone and strength; and the total area of blood space is increased, owing to paretic dilatation of the smaller vessels. In such a condition here presented the failing circulation is due not so much to the disease *per se* as to vitiated anatomical structure and physiological function, and the indications for treatment are plain. The prime object to be desired is the restoration of the function of the spinal cord, reflex centres, and nerve-endings. A drug that will do this causes a cessation in the destruction of tissue and less waste, thereby minimizing the drain upon the nutritive elements of an already deteriorated blood; vaso-motor tonus returns, the arterioles and capillaries contract, the superabundant vascular space disappears, and hence a larger amount of blood passes through the heart at each cardiac cycle, stimulating its action and promoting its nutrition.

Strychnine seems to fulfil all the indications in the morbid condition above described, for the action of this remedy being expended upon the spinal cord and this part of the nervous system in conjunction with the sympathetic playing so important a *rôle* in repairing and maintaining the various processes of organic life, it is natural to infer that an intelligent stimulation of its functional activity would, under such circumstances, be a perfectly logical procedure, provided no structural lesion existed in its substance. Clinical experience seems to have established the truth of this reasoning, and Dr. Bradfute extends this evidence with the report of several cases in which symptoms of profound collapse were overcome by the use of strychnine. Its administration must, however, be guided by the effect produced. $\frac{1}{60}$ grain of the sulphate may be given hypodermically every two hours, or oftener if necessary, until there is the desired response. It is interesting to note that in such a condition of the system large amounts are easily borne, especially if the patient has been taking large amounts of alcohol, and the author states he has given as much as four grains in twenty-four hours without producing toxic symptoms. The failing circulation of diphtheria is a typical one for the exhibition of strychnine, for in this affection in its severer forms we have all the conditions present to which its action is antagonistic.

TERPENE IODIDE IN ACUTE DISEASES OF THE LUNGS.

The great disadvantage that the physician has to contend with in the administration of medicines is the changes that they are liable to undergo when taken into the stomach before they finally enter the circulation. It would, therefore, appear that all our remedies should be administered hypodermically, but this method has numerous objections, principally on account of the pain produced and the after-effects which may follow.

In a paper published in the *New York Medical Journal* for February, 1891, Dr. William H. Gregg maintains that terpene iodide enters into the circulation unchanged, and when administered by the stomach acts quite as quickly as if it were administered hypodermically, is a powerful antiseptic, is comparatively harmless, is free from unpleasant after-effects, and the author maintains that in many cases of acute pulmonary disease, more particularly acute congestive pneumonia, and those catarrhal and throat affections which are so often the premonitory symptoms of more serious mischief, the disease may be cut short by the administration of the terpene iodide. In acute affections of the throat he recommends its use in spray, while in other cases it may be given to adults in 10 drop doses, on a teaspoonful of sugar, once or twice a day,—in the morning and at bedtime. The morning dose should be followed by a glass of milk or bouillon, while larger or more frequent doses are apt to produce marked diuretic effects.

THERAPEUTICS OF BENZO-PHENONEID.

According to the Paris correspondent of the *Lancet* for January 10, 1891, M. Galezowski read, on the 27th ult., to the Société de Biologie, a communication on the application in ophthalmology of this new bactericide, discovered by him and M. Petit. They have succeeded in producing, by the decomposition of an aniline dye, a definite compound (tetramethyl-diapsido-benzo-phenoid), which they propose to call by the less formidable name of benzo-phenoneid. This product is endowed with the same powerful microbicide properties as pyoktanin, whose chemical composition is unknown. Soluble in 100 parts of water, the solution, further diluted a hundredfold, is neither caustic nor irritant. Applied locally, it has proved very efficacious in

causing the rapid and painless cicatrization of ulcers of the cornea which had resisted all other methods of treatment. It has given also good results in purulent keratitis and chronic phlyctenular ophthalmia.

BUTYL CHLORAL IN THE TREATMENT OF FACIAL NEURALGIA.

According to BOCQUILLON (*Journ. de Méd. de Paris*, December 28, 1890) butyl chloral administered internally produces sleep, but without the disadvantage of causing any slowing of the pulse or respiration, and without producing any unfavorable after-effects on the digestive or other organs.

The general evidence seems to indicate that when simple insomnia is to be combated, butyl chloral may prove efficacious, but when an anæsthetic effect is produced, it is of little value. Nevertheless, numerous authors have recommended butyl chloral as a most efficient remedy in the treatment of facial neuralgia, when administered either in the form of solution or in pill form or enemata. Subcutaneous injection should not be employed, as it leads to production of abscess. The author recommends its administration in the form of solution containing 10 parts each of hydrate of butyl chloral and 20 parts of glycerin in 120 parts of distilled water. A teaspoonful of solution contains about fifteen grains of butyl chloral, and may be administered in the dose of 1 or 2 teaspoonfuls daily.

THE ACTION OF THEBAINE, NARCOTINE, AND CERTAIN OF THEIR DERIVATIVES.

With a view to extend our knowledge as to the relation between chemical constitution and physiological action, DR. RALPH STOCKMAN and MR. DOTT have made a number of experiments with various of the opium alkaloids and their results, which prove that the addition or substitution of certain radicals modifies very superficially the original action of the alkaloid (*British Medical Journal*, January 24, 1891). Their experiments commenced with the study of thebaine, which is regarded as a vinyl ether of morphine, just as codeine is the methyl ether. This alkaloid is in many cases the most poisonous of the opium alkaloids, and its physiological action, which closely resembles that of strychnine, with the addition of a distinct narcotic stage, has been well established by Claude Bernard and numerous observers.

The authors' experiments on this alkaloid were principally as to the action of the methylthebaium, which is an addition product formed from thebaine. These experiments show that the physiological action of thebaine is not profoundly altered by the addition of methyl sulphate.

Its tetanizing power is much diminished, while its paralyzing actions on the spinal cord and on motor nerve terminations are greatly increased. Sulphate of methylthebaium may clearly be included in the morphine group, as it induces a narcotic and a tetanic stage. The narcotic stage, like that of thebaine itself, is (in mammals, but not in frogs) extremely ill-defined, its most prominent action, especially in mammalia, being paralysis of motor nerves. But when special methods of investigation are used, its close physiological relationships to thebaine and to morphine can be readily demonstrated.

Similar experiments were also made with narcotine, hydrocotarnine, and cotarnine, the result showing that the chemical derivatives alter their action in degree but not in kind. It thus would seem that the chemical change represented in these three substances does not alter the similarity of their action, but simply affects their dosage, while no radical change of action is produced in them by the chemical change of constitution. This has already been shown to be the case with morphine, and it is also new that the same holds good in other alkaloids, such as cocaine and caffeine.

THE EMPLOYMENT OF PILOCARPINE IN AURAL AFFECTIONS.

The favorable results obtained in a series of cases of severe eye-affections, particularly of acute irido-cyclitis, hemorrhages into the anterior chamber of the eye, and opacity of the vitreous body, induced PROFESSOR POLITZER to give pilocarpine a trial in several cases of labyrinthine affection of syphilitic nature.

The rationale of this method was that in virtue of the rapidly-occurring change of matter, the reabsorption of unorganized exudation products might be brought about. The results of this experiment were so satisfactory that, at the Second Otological Congress, in 1880, he recommended a continued trial of this method in cases of recent affections of the labyrinth. In the *Lancet* for

January 3, 1891, Professor Politzer writes that since that time he has employed subcutaneous injections of pilocarpine in every variety of recent and chronic affections of the labyrinth, the results obtained by himself and others being so favorable that the value of muriated pilocarpine in labyrinth affection must not be underestimated.

He states that he has been in the habit of using a two per cent. solution, 2 drops of which are injected subcutaneously in the forearm, and the dose gradually increased, a drop at a time, to eight. Following rapidly upon the injection, there is a considerably increased secretion of saliva and sweat, which ceases after the lapse of from thirty to forty-five minutes. Rarely it is accompanied by disagreeable symptoms, such as nausea, vomiting, giddiness, fainting, collapse, spasm of the bladder, which can be antagonized by taking from 2 to 3 drops of sulphate of atropine, 7 grains in 160 minims of water. The injections are to be made daily. If, after the lapse of a fortnight, the use of this remedy does not produce an improvement in hearing, it must be regarded as ineffectual and be abandoned. But if, on the other hand, an early and distinct improvement in hearing can be observed, the injections should be continued as long as there is a progressive increase in the faculty of hearing to be elicited upon examination. The period in which the maximum of the hearing distance is attained varies from six to forty days. It is to be noted that the increase in the hearing power is rarely regularly proportional, since it is usually most rapid in the first week or fortnight, while in the subsequent course of the treatment it progresses very slowly. In rarer cases the reverse is true, the hearing power at first increasing slowly and later more rapidly.

Vacillations in the hearing distance are not infrequently observed in the course of treatment, a rapid improvement of several days being promptly followed by a rapid diminution of it, lasting also for some days. The use of subcutaneous injections of pilocarpine, which was at first limited to syphilitic diseases of the labyrinth, was extended later also to those cases of deafness which were found to be dependent upon an affection of the auditory nerve apparatus. This proceeding was indicated by the rapid development of deafness apart from any discoverable anatomical damage in the middle ear, and confirmed by the result of the examination with the tuning-fork, the latter affording important indications for the employment of pilocarpine. If the examination with the tuning-fork proves that in a case of extreme deafness the sound is heard perceptibly longer opposite the ear (ear conduction) than from the mastoid process (positive experiment of Rinne); also that low tones are better perceived by air conduction than high ones; and, lastly, if there is a history of symptoms pointing to the implication of the labyrinth, such as giddiness or total inability to hear the ticking of a watch through the head-bones, then the existence of an affection of the labyrinth is very probable, and it is in such a case that the subcutaneous injection of pilocarpine should be employed.

Dr. Politzer but rarely uses subcutaneous injections of pilocarpine in acute inflammation of the middle ear, although he refers to several cases of acute inflammation of the middle ear in which perforation had not taken place, and where a protracted treatment failed to produce reabsorption of the exudation products lying in the cavity, and where, after three or four subcutaneous injections of pilocarpine, a constant improvement could be observed. Further, the author recommends the subcutaneous injection of pilocarpine in those cases of acute suppuration of the middle ear in which perforation of the tympanic membrane has occurred, and in the course of which deafness supervenes, dependent upon some complication of the labyrinth. Within recent years Professor Politzer writes that he has used muriated pilocarpine, locally injecting from 6 to 8 drops of a two per cent. warm solution through a catheter into the Eustachian tube and tympanic cavity. When it is employed no unpleasant results occur. It is but rarely that salivation and diaphoresis are observed. In chronic catarrh of the middle ear he injects pilocarpine in the tympanic cavity, particularly in those cases where the power of hearing is distinctly improved after inflammation of the middle ear, and where a slight swelling in the Eustachian tube can still be discovered upon examination.

The object of the local application in these cases is to bring about a slight reaction in the mucous membrane of the middle ear, and in this way to cause the absorption of inflammatory products. And, as a matter of fact, in some particular instances, the improvement of hearing following these injections has been more pronounced than that obtained by the use of ten per cent. solutions of soda, which until now have been most fre-

quently employed. On the whole, the cases in which the local injections of pilocarpine produce a notable result are but few; in most cases the faculty of hearing does not improve at all, or the improvement is only indifferent and of short duration. Here, too, the treatment must not be extended beyond two or three weeks. It is quite otherwise with the so-called cases of chronic catarrhs in the middle ear, where the adoption of this method of treatment must be deprecated, and in the treatment of dry catarrh of the middle pilocarpine is worthless. So, also, Dr. Politzer insists that in every case of extreme deafness, where the tuning-fork can be heard longer over the mastoid process then opposite the ear, and in addition where low tones are not at all or only faintly perceived through the medium of the ear, while high tones are at the same time very distinctly heard, the subcutaneous application of pilocarpine is very strongly contraindicated. Finally, the author summarizes his conclusions as to the use of pilocarpine in aural troubles as follows:

1. The subcutaneous injections of pilocarpine are particularly indicated in recent affections of the labyrinth, be they of a syphilitic nature or not. In protracted diseases of the labyrinth these injections, if tried, must be abandoned if no improvement results after from ten to fifteen injections.

2. The subcutaneous injections of pilocarpine are but rarely employed in otitis media acuta, where the cavum tympani contains hardened exudative products, which resist reabsorption; moreover, in panotitis gemina diphtheritica, or in other diseases produced by infection.

3. The subcutaneous injections of pilocarpine are decidedly contraindicated in cases of dry sclerotic catarrhs of the middle ear.

4. Injections of several drops of a two per cent. solution of muriated pilocarpine through the catheter into the tympanic cavity are beneficial in some cases of catarrhs connected with swelling and a slight secretion of the mucous membrane of the middle ear, continued from one to three weeks alternately, with inflations or air by Politzer's procedure. The purpose of the present communication is to reduce to a just measure the therapeutic value of the subcutaneous injection of muriated pilocarpine in diseases of the ear, and to draw attention to the frequent abuse which has been made of this remedy for some time past.

POISONING FROM THE INSTILLATION OF HYDROCHLORATE OF COCAINE IN THE MIDDLE EAR.

According to Dr. Ficano (*La Pratique Médicale*, January 6, 1891) accidents due to the absorption of cocaine by the various methods by which this medication may be introduced are not rare. Cases of this nature, which, however, follow the simple dermic application of non-poisonous doses, must be due to idiosyncrasy of the individual and are not to be explained. But few cases are, however, on record where poisonous symptoms have followed its administration through the external ear, even although it must have occurred in numerous instances, for cocaine is probably the first remedy which would now suggest itself to relieve a rebellious earache, even although it is claimed that there is no absorption by the external auditory meatus. When the drum-head is perforated, then, of course, the remedy comes in contact with the mucous surface, and its rapid absorption may then be expected.

The case reported by Dr. Ficano was that of a woman, 43 years of age, who had for some time suffered from intolerable tinnitus, which accompanied a dry otitis media, with diminution of hearing. A few drops of a five per cent. solution of cocaine were introduced into the middle ear by means of a catheter, after use of the Politzer method of insufflation. In a short time vomiting came on with cramps and diarrhœa, a condition which continued for several hours. The symptoms, the author stated, were analogous to those of sea-sickness, and he offers a number of hypothetical explanations as to the way in which these results might be produced. Whether by modifying the quantity of liquid in the middle ear it also modified the audo-labyrinthic tension, or whether, by causing retraction of the tympanic mucous membrane, it causes a compression of the labyrinth through the oval window. Marked muscular inco-ordination was one of the symptoms produced, and the author believes this indicates disturbed equilibrium in the liquids of the internal ear.

THE TREATMENT OF CHRONIC DIARRHŒA BY MEANS OF REST AND MASSAGE.

One of the most notable features in all cases of chronic diarrhœa is the atony of the muscular coat of the stomach and intestines, and one would be almost inclined to believe

that the first tissues to suffer from the malnutrition, resulting from the diminished absorption, are the walls of the gastro intestinal tract themselves. Probably this condition of affairs is brought about by the development of alkaloids, the products of albuminous decomposition, while to the absorption of these alkaloids may be attributed not only the nervous symptoms, so frequently accompanying chronic diarrhœa, but in some degree the resulting anæmia, fatty degeneration, or emaciation observed in these cases. It is, however, undoubted that in the latter and more chronic developments of the malady there is an atonic and atrophied state of the stomach, involving both the mucous and muscular coats, with consequent diminished absorption and muscular action, so that the food remains in the stomach for a longer period than is necessary for the normal processes of digestion, while the gases resulting therefrom are not subjected to the pressure normally exercised upon them by the heavy muscular coat of both stomach and intestine. As a consequence of this, the action of the gastric juice upon proteids is extended, with the result that digestion continues beyond the normal formation of peptone; and the importance of this point is especially emphasized in a paper entitled "The Treatment of Chronic Diarrhœa by Rest and Massage," published by MR. A. SYMONS ECCLES, in the *Practitioner* for December, 1890, and January, 1891. He has found that artificially-peptonized milk, if the action of the peptic solution be allowed to continue until there is a distinct bitter taste produced in the milk, be then administered to a patient suffering from chronic diarrhœa, flatulence, intestinal colic, and a loose, offensive discharge almost invariably follow within two or three hours. The duration of gastric digestion may be estimated by what is known as the salol test, which consists in administering salol with the food, and the appearance of salol in the urine may be fairly accurately regarded as indicating the termination of gastric digestion. In cases of chronic diarrhœa, no improvement in body-weight will ordinarily be observed as long as the test fails to give the reaction of salol in the urine within three hours, and the diarrhœa may thus be regarded as the result of diminished absorption in the intestines, and this diminished absorption may be measured by the absorption of salol. Salol is insoluble in acid solutions, while it is readily soluble in alkaline media. The average time in health elapsing between the ingestion of salol and its appearance in the urine is forty-five minutes, and if there be delay in the appearance of salol in the urine it follows that there has been interference in its absorption from the intestine. The premises, therefore, on which the author bases his theory for the use of massage and rest is that, in the first place, there is atony of the stomach, and consequently undue prolongation of the time which food remains in the stomach; there will be in many cases excessive acidity of the gastric secretions, and as a consequence the proteids break down into the leucin, tyrocin, and various other substances more or less of an irritating character, and perhaps lead to the production of poisonous leucomaïnes and ptomaïnes. If any means can be devised to prevent the undue prolongation of the time during which food-stuffs remain in the stomach, and thus to limit the duration of peptic digestion, and so diminish the formation of gas, much may be effected towards the elimination of poisonous alkaloids and the absorption of soluble matters.

In all cases unquestionably *rest* is an important factor, and in this connection the term rest is used in its most comprehensive sense to imply not only the absence of muscular or bodily fatigue, but of all such conditions as cold, hunger, business worry, or domestic anxiety. It may not be so difficult to insure for the patient physical and even physiological rest, but it is not always easy to compel mental quietude, depending, as it does, on external influences frequently beyond the control of patient and physician alike. It is, therefore, of no small importance to urge upon the patient the necessity of placing himself as far as possible under conditions affording the least temptation to indulge in mental or emotional activity, and, without suggesting isolation, it is certainly something in favor of a successful result if the physician can assume a control over the communications between the patient and the outer world, which can thus be modified according to the individual requirements of the case.

So far as physical rest is concerned, the recumbent position in a warm bed must be enjoined. In many cases of chronic diarrhœa it will be found that, after the acute stage has passed, patients have not been enjoined to spend a lengthened period in a recumbent position, and some who have not already reached a condition of serious cachexia are somewhat averse to the rigorous adoption of absolute rest. But so far as the experience of the writer goes, the most assured success

has followed treatment in which, for the first few weeks at all events, the patient has been kept in bed.

An *equable surface temperature* appears to be necessary to the successful treatment of these cases, and until the powers of assimilation have been regained, and thus the nutrition of the body re-established, the most convenient way by which to insure the absence of cold impressions on the skin is to promote the existence and maintenance of a layer of warm air enveloping the surface of the body.

To those for whom the constant drain of frequent relaxation of the bowels for many weeks or months has rendered muscular activity well-nigh impossible, or to be undertaken only with the certain consequence of extreme fatigue and exhaustion, absolute rest under careful supervision is not objected to as irksome. Physical rest and bodily warmth being obtained, so far as external means will allow, the next point is to maintain the physiological rest of the gastro-intestinal canal, and the very existence of diarrhœa is in itself the symptom of pathological unrest, which, however, may be greatly modified by the quality and quantity of the ingesta ; but before any particular practice can be initiated it is necessary first to ascertain as soon as possible the nature and locality of the disease from which the patient is suffering, hence the great importance of the scientific test of the state of digestion, and this the author believes we possess in the salol test. Its employment in cases of chronic diarrhœa will confirm the presence of some condition which greatly interferes with the free and rapid assimilation of food. When administered at regular intervals, its excellence as a clinical method of determining the effects of treatment, as well as guiding us in the choice of diet and the employment of remedies, can hardly, in the author's opinion, be overestimated. Frequent manipulation of the abdomen also enters very largely into the author's plan of treatment. The duration of the local manipulations necessarily depend very largely upon the individual requirements of each case, and no mere routine treatment will serve to attain the desired result.

The cases of chronic diarrhœa in which the writer has found massage valuable present certain clinical features sufficiently marked to permit of their classification, the different forms being distinguished from each other by characteristic symptoms. While, with the exception of a few of a less serious type, they all exhibit signs of enfeebled digestion, anæmia, emaciation, and debility, the nature of the evacuations affords a readily distinguishable and rational classification of the malady. In lienteric diarrhœa, for instance, as its name implies, the stools afford undeniable evidence of the passage of food-stuffs which have undergone little or no digestion either in the stomach or intestines, colic and diarrhœa often supervening rapidly after taking a meal, when the predisposition to diarrhœa has existed for some time. In these cases it is often found useful to employ systematic massage of the abdomen before a meal, the manipulations being initiated by somewhat vigorous rubbing over the hypochondriac and epigastric regions, followed by careful kneading over the whole abdominal wall. Much of the success of the treatment appears to depend upon the altered conditions of circulation induced by general corporeal massage. In the chronic diarrhœa depending upon climatic influences the application of massage shortly after meals is indicated, and frequently it is necessary to employ it soon after each meal.

In the earlier stages of the treatment of sprue, the abdomen needs frequent gentle and prolonged manipulations, and these should be employed daily with assiduity until the evacuations cease to exhibit their well-known abnormal character.

Finally, the author sums up his conclusions as to the effects of kneading the abdomen in such cases as follows :

1. The generation of gas within the stomach and intestines is diminished and its expulsion effected.

2. The onward movement of the gastro-intestinal contents is favored.

3. The rapidity of circulation through the visceral lymph- and blood-vessels is increased.

4. The circulation through the liver is improved, and thus the destruction of alkaloids by this organ is promoted. In this connection perhaps not the least valuable effect produced by abdominal massage is the stimulation to more vigorous action of the diaphragm and the consequent automassage, if one may so describe it, produced by the deeper inspirations and abdominal reflexes excited by the earlier manipulations of the abdominal wall.

5. The abdominal vascular area is dilated.

6. The rate of absorption from the intestines is increased.

7. The intestinal nerves are stimulated.

ON THE ACTION OF ATROPINE IN DISEASES OF THE HEART.

Dr. Cardarelli has experimented with atropine in sixty-five cases of various forms of functional cardiac disease, measuring the pulse with the chromograph of Verdin and the arterial pressure with the sphygmomanometer of Basch. His conclusions, which appear to be based on a most careful study, are published in *La France Médicale*, January 23, 1891:

1. Atropine, in doses of $\frac{1}{120}$ to $\frac{1}{80}$ grain, given hypodermically in man, manifests itself first in its action on the heart.

2. The action of atropine on the heart consists in the overcoming to a greater or less degree of the inhibitory influence of the vagus nerve.

3. As a consequence of this paralyzing action on the vagus, there is constant acceleration of the cardiac rhythm, which may be in certain cases accompanied by a slight transitory slowing.

4. Arterial pressure is reduced under the influence of atropine in direct proportion to the acceleration of the rhythm.

The author concludes with the statement that, when a clinician cannot use atropine in slight forms of irritation of the pneumogastric, in which there is no slowing of the pulse, it will be, nevertheless, a great error not to prescribe atropine in cases where a permanently slow pulse is accompanied by epileptiform vertigo, and, above all, by syncope.

THERAPEUTIC ACTION OF CAMPHORIC ACID.

The therapeutic value of camphoric acid in acute and chronic catarrhs of the respiratory mucous membrane, acute and chronic cystitis, and in the night-sweats of phthisis has recently been the subject of study in the medical clinic at Griefswalder, under the direction of Dr. Hartleib, whose results are furnished in the *Centralblatt für Klinische Medicin*, No. 5, 1891.

The drug was administered in the form of an alcoholic solution, 1 part of camphoric acid in 11 of alcohol, in glycerin solution, and in aqueous solution with the addition of bicarbonate of sodium. In angina of various forms, one-half to one per cent. solutions were employed as a gargle and as a local application, but the remedy appeared to possess no advantage over the drugs used for the same purpose in chronic bronchitis and in pulmonary tuberculosis, though some patients claimed to receive some relief from its employment. Very favorable results, however, are claimed to have followed its employment in cases of chronic cystitis, three out of five being absolutely cured within three to six weeks, the remedy in these cases being employed in one-half per cent. solution, with which the bladder was washed out twice daily. Stronger solutions than one per cent. cause too much irritation and should not be used, although the author recommends the plan of washing the bladder with eight grains, given three times daily. It also produces more favorable results in the treatment of the night-sweats of numerous phthisical cases, while unfavorable after-effects were never noted.

BROMISM AND INTESTINAL ANTISEPSIS.

In a note read before the Société de Biologie, at the meeting held January 24, 1891, Dr. Ferret continues the study of the influence of intestinal antisepsis on bromism, already referred to in a previous number of the Gazette (*La Médecine Moderne*, February 5, 1891). He confirms the statement already mentioned that not only may one with sufficient doses of naphthol and salicylate of bismuth prevent cutaneous manifestations of bromism, but one may by these means even cure an eruption, if already so produced. He also maintains that borax also may produce eruptions quite as serious as those which follow the administration of large amounts of bromides, and that such eruptions may be likewise treated and cured by the same method. He believes that his experience has demonstrated that this method should be generally employed, and always with a prospect of success in the treatment of the cutaneous manifestations which follow the ingestion of drugs.

Reviews.

Principles of Surgery. By N. Senn, M.D., Ph.D. Philadelphia and London: F. A. Davis, 1890.

Our author has well said in his preface, that "the successful study and practice of any branch of the healing art require a thorough knowledge of the principles upon which it is based." How many mistakes might have

been avoided, how much suffering might have been saved, if a more thorough knowledge of the principles which govern our art had been learned rather than the too hasty desire to acquire a knowledge of the practical part of surgery! Not that the latter is to be underrated, but that its application would be so much more advantageously utilized if the former was more fully understood. The surgeon who is able to answer the why and wherefore is the one who may be relied upon, and Professor Senn has well expressed it as follows: "The student who has mastered the principles of surgery will have no difficulty in applying his knowledge in practice, while the one who has burdened his memory with numerous details, to meet special indications, is always at loss in making prompt and judicious use of his therapeutic resources when confronted by rare lesions or unexpected emergencies."

During the past decade or two the number of American and English works which treat of surgical diseases have been not a few, and their excellency cannot be questioned. In no branch of medicine has there been such progress made, and the results obtained have been far beyond the expectations of the most sanguine; yet, with it all, there has been a more or less deficiency, even in the most recent of these works, in the fundamental principles which are the true reasons for the progress and success of the art and science of surgery. Our etiology and pathology of surgical diseases at the present time cannot be compared with that of fifteen or twenty years ago. New etiological factors have been discovered, and new pathological indications have been demonstrated; new names have been added, and new therapeutics are called for; indeed, the surgeon who has not been a constant student of his profession will scarcely be able to comprehend the recent literature which treats of the art and science of surgery.

As an evidence of the change which has taken place in the use of new terms to express the progress made in surgery, we will refer to Professor Senn's first chapter, which treats of "Regeneration." This is defined as "a multitude of processes, which are intended to repair the normal physiological waste of the tissues in the living body, or to restore tissues lost by injury or disease." Regeneration is not inflammation, and they are said to be entirely different processes. "An ideal regeneration takes place without inflammation, provided the seat of injury or tissue-destruction remains aseptic,—that is, free from pathogenic microbes."

The regeneration or reparative process, in the healing of wounds, is stated to "consist of homologous cell-development, and the new tissue resembles, anatomically and physiologically, the fixed cells from which it is produced,"—this is to say, epithelial cells are only developed from epithelial cells, nerve-tissue only from nerve cells, and the same law is universal throughout the entire body. It is the fixed cells of the tissues only which take part in the healing of wounds. The immediate or direct union of wounds is not admitted by our author. He writes: "A certain amount of coagulation necrosis takes place in every wound, and the material thus formed serves as a cement-substance, which temporarily glues the parts together." The healing of wounds by primary intention is considered always to occur whenever there is no suppuration, either without or with visible granulation tissue. And, again, "All wounds which heal without suppuration heal without inflammation. All inflamed wounds suppurate; the reparative process is delayed until the inflammation has subsided." These principles being admitted, it follows that the proper classification of the healing of wounds is such as Professor Senn makes,—viz., "(1) aseptic wounds and (2) infected wounds." An aseptic wound is said to be one "not contaminated with pathogenic micro-organisms,—heals without inflammation." The *rôle* which the leucocytes play in the healing of an aseptic wound is that they "serve a useful purpose in the temporary closure of divided capillary vessels, and in the formation of temporary cement-substance, by which the surfaces of the wound are mechanically glued together; and, lastly, as food for the embryonal cells; *but they take no active part in the production of new tissue.*"

In order to comprehend the healing of wounds, and the process of regeneration, it is very evident that the histological changes which take place in the tissues must be understood, and the laws which govern the formation of new tissue are to be remembered; therefore, a study of the multiplication of cells, and the process by which it is accomplished is imperative. In this connection the author has given a description of karyokinesis, which should be thoroughly mastered by the student. While admitting that the direct cell division may at times be a method of cell-multiplication, in the healing of wounds, yet it is the indirect cell-division, or karyo-

kinetic process, which is most frequently met with; and, further, wherever the latter process is seen, "it is positive evidence that the fixed tissue-cells are the seat of tissue-proliferation, and that wounds are healed and defects repaired exclusively by this method of cell-formation."

In the treatment of wounds, from the earliest times until the present period, it has been the great aim of all surgeons to obtain their healing by the process of union by first intention. Professor Senn gives us some most excellent, as he terms them, "positive indications in the treatment of wounds, with special reference to secure union by first intention." "Absolute asepsis," he says, "can only be secured by strictest antiseptic measures. Surgical cleanliness is more than ordinary cleanliness." All bleeding in a wound is thought to be objectionable, and therefore most careful hæmostasis should be observed. Accurate suturing, not only of the edges of the wound, but muscle to muscle, nerve to nerve, tendon to tendon, is an indication of great importance, and it should be most carefully done; all cavities are to be closed and as perfect approximation as possible is to be sought after. Drainage is very properly said to be necessary only when the surgeon is at all in doubt as to whether the wound is aseptic or not. If aseptic, drainage is unnecessary and may be dispensed with; physiological rest, in the after-treatment of a wound, is looked upon as of the greatest importance, and it should be secured as far as possible.

The "Regeneration of Different Tissues" is considered in chapter ii., and Professor Senn here more emphatically gives his views in regard to the *rôle* played by the different cells. He writes: "No positive proof has yet been furnished that the leucocytes, or any of the cellular elements of the blood, take any active part in the restoration of the lost parts." It is the homologous cell-proliferation which seems more rational than to suppose that the indifferent white blood-corpuscle is ever converted into the tissue-cells of a part. The organization of the thrombus, in a ligated blood-vessel, by the histological elements of the thrombus, is denied. Thus "the blood-clot always occupies only a passive *rôle*, and, if present, is only in the way of a speedy definitive closure, which invariably is effected by proliferation from the fixed cells of the vessel-wall." In the regeneration of bone it is the medullary tissue of the osseous structure which produces the permanent callus and the cell-proliferation from the periosteum which forms the provisional callus. In other words, bone is regenerated from bone-cells only; but the cells of the periosteum are capable of bone formation, yet such formations are not permanent. This has been shown by the investigations of Ollier, who found that the transplanted periosteum was first changed into cartilage, which was later transformed into bone, but such bone formations disappeared again, unless they formed in a place where bone normally existed.

Chapters iii. and iv. treat of "Inflammation." True inflammation is believed to be always caused by the presence of one or more kinds of pathogenic microbes. It is the series of histological changes which occur in the living body from the presence and action of specific micro-organisms; while, on the contrary, regeneration is the histological changes which take place in the tissues, which have been primarily in an aseptic condition, or have been rendered so after the inflammation has subsided. Professor Senn has wisely not attempted to make a definition to express what is meant by the term inflammation. Our present knowledge of the causes, the anatomical changes, and the pathological characteristics of the process he does not think sufficient to warrant the attempt. "The conception of the true nature of inflammation, for the present, at least, must remain symptomatic." These chapters on inflammation are full of most interesting and important questions, both for the student and surgeon. Space, however, will not permit us to dwell too long upon them. They should be carefully read and thoroughly understood by all students of medicine. We will call attention to the section on "Phagocytosis," which is the process by which leucocytes and other cells remove dead material, and destroy or digest pathogenic micro-organisms. This process has not been accepted by all writers, and, indeed, it has met with considerable opposition. As a theory, it has much to recommend it. As a fact, it has not yet been truly established, but it has many arguments in its favor. The conclusion given by our author we think quite just. He writes: "From a practical stand-point it can be said that all therapeutic measures which influence favorably the process of phagocytosis, in the broadest meaning of the word, are calculated to exert a potent influence in arresting or limiting infective processes."

Inflammation not being considered a disease *per se*, but rather an effort on the part of the

organism and affected tissues to eliminate, or rather render inert, the primary cause, its treatment must necessarily be symptomatic. In surgery, it is the prevention of the action of the cause which is to receive the greatest attention, and we have seen that the cause is always some form of pathogenic microbe; therefore prophylactic treatment by strict antiseptic precautions is the fundamental principle which is to govern us in our surgical practice.

The elucidation of the subject "Pathogenic Bacteria" is most ably and clearly given by Professor Senn, in so far as it is connected with surgical pathology. The necessity for a study of this subject is only too evident; indeed, when it is considered that most forms of inflammation are due to some specific micro-organism, a knowledge of their history, their method of development, and the means necessary for their detection becomes absolutely essential.

Inflammation being always due to some form of micro-organism, one of its terminations is in suppuration, and the latter is defined by Professor Senn as "the process by which the morphological elements of the inflammatory product, the leucocytes and embryonal cells are converted into pus-corpuscles." This change of these cells into pus-corpuscles is stated to be "caused by the action upon the tissues of specific micro-organisms,—the pus-microbes,—and the transformation of leucocytes and embryonal cells into pus-corpuscles is accomplished by the same cause." From this it is seen that the indirect cause of suppuration is thought to be the condition produced in the tissues by the inflammation; the direct cause is the presence of pus-microbes, which act on the leucocytes and embryonal cells, transforming them into pus-corpuscles. The consideration of the important question as to whether it is possible to have suppuration without the presence of pus microbes, is answered by our author in the affirmative; but such a form of suppuration is termed chemical, and differs from clinical suppuration in that it is a sterile and aseptic pus, and is not progressive in its action. On the other hand, clinical pus is due to the presence of pus-microbes; "they are the immediate and essential cause of suppurative inflammation." In regard to the *rôle* played by the ptomaïnes, as an etiological factor in suppuration, the author, we think, very justly says, "To the practical surgeon it is immaterial to know whether the transformation of leucocytes and embryonal cells is brought about by the direct action of pus-microbes, or by the ptomaïnes which they produce in the tissues."

Septicæmia is said to be closely related to pyæmia, both clinically and etiologically, and it is thought to be due to the introduction into the circulation of septic micro-organisms or their ptomaïnes. From a study of the bacteriological researches of many investigators, Professor Senn concludes "that the essential bacterial cause of septicæmia is variable, and that the disease represents a general febrile condition, which is brought about by the absorption from a local focus of different toxines from as many different microbes;" and again he writes, "This disease can be produced by any of the microbes, which, after their introduction into the organism, have the capacity to produce a sufficient quantity of phlogistic ptomaïnes to give rise to septic intoxication."

The fact that bacteriological investigations have demonstrated the presence of some of the forms of pus-microbes, in all cases of pyæmia, justifies the definition of this disease as an affection "caused by the entrance into the circulation of pus or some of its component parts." Any of the pyogenic microbes are said to have the power of determining an attack of pyæmia, provided they are present in sufficient quantity in the blood. It is not the kind of pus-microbes which have caused the primary suppuration that gives rise to the pyæmia, but it depends more upon the location and anatomical structure of the tissues in which the primary infection has occurred. The cause of pyæmia being now admitted,—viz., pus infection,—its treatment resolves itself into prophylactic measures. "The prevention of suppuration in a wound furnishes absolute protection against pyæmia."

The remaining chapters of the book treat of "Erysipelas," "Tetanus," "Hydrophobia," "Tuberculosis," "Actinomycosis," "Anthrax," and "Glanders." In concluding our notice of Professor Senn's book, we feel that we have not done him justice in the above brief review. The work is a most valuable one; in fact, we are inclined to consider it the most important publication, in connection with surgery, that has been issued for some years past. No surgeon, no matter how great his experience, can read the book without being better able to practise his profession, and no student of medicine should be permitted to assume the duties of a surgeon without having thoroughly mastered the principles here given. J. H. C. S.

MEMORIAL SKETCHES OF DR. MOSES GUNN. By his wife.
Chicago: W. T. Keener, 1890.

The history of a noble man and enthusiastic surgeon, faithfully depicted by his wife and friends, consisting largely of extracts from his letters, delightfully woven together so as to make a charming story without a break. His letters from the seat of war, especially during the Peninsular campaign under McClellan, when he acted as surgeon to the Fifth Michigan Regiment, are exceedingly interesting, and his enthusiastic admiration for the commander-in-chief, with his affection for the President, are typical of the feelings of the entire army during this exciting time. His letters from Europe during the summer of 1879, and again in 1881, are well written and amusing. Dr. Gunn was for many years Professor of Surgery in Ann Arbor University, and was, besides, an active surgeon.

These sketches will be found of interest to the general reader, as well as to his friends and to the medical profession at large.

THE PATIENT'S RECORD, FOR THE USE OF PHYSICIANS AND NURSES. Compiled by Agnes S. Brennan.
New York and London: G. P. Putnam & Sons, 1890.

This book is ruled so that an exact record can be kept of the temperature, pulse, respiration, medicine, nourishment, stimulants, amount of urine passed, defecation, the time of day on which the observations were made, remarks on the case, and the doctor's orders from day to day, and will be found useful in the sick-room. It also contains a number of temperature charts for the use of physicians. The paper is good and the lines distinct. It is bound in boards, with leather back and edges, and on the back cover is a leather loop to hold a pencil.

TRANSACTIONS OF THE MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF MARYLAND. NINETY-SECOND ANNUAL SESSION, APRIL, 1890.
Baltimore: Griffin, Curley & Co., 1890.

The transactions of the ninety-second session contain several valuable papers, which will repay the reading, among which may be cited "Some Practical Points in Hernia," by R. W. Johnson; "Double Popliteal Aneurism cured by Ligature," by J. E. Michael; "Rachitis considered in Regard to some of its Symptoms," by William Lee; and "The Early Detection of Pulmonary Consumption," by William Canfield. In this paper Dr. Canfield demonstrates the clinical importance of the early recognition of the disease by examining the sputa for the bacillus tuberculosis after it has been stained by a rapid process. He prefers a coloring fluid of fuchsine (1 part), absolute alcohol (10 parts), and a five per cent. solution of carbolic acid (100 parts). The clinical value of the early detection of tuberculosis is undoubted, and will become more so if the "Koch lymph" should prove a specific in this disease.

In addition to other papers of value and the minutes of the meeting, reports of various committees, and the papers presented to the various sections will prove interesting.

ESSENTIALS OF PRACTICE OF PHARMACY. By Lucius E. Sayre, Ph.G., etc.
Philadelphia: W. B. Saunders, 1890.

This is No. 18 of Saunder's Question Compends, and, like all of its predecessors, is arranged in the form of questions and answers, which, while it is apt to catch the eye of the student, is nevertheless of more than doubtful utility. After an experience of many years in medical teaching, we are fully convinced that books of this kind, far from being of advantage, are really harmful to the majority of students, who, instead of using them as they should be used,—viz., to review knowledge already acquired,—study them, to the exclusion of the larger and consequently more thorough text-books. As, however, there is a demand for such books, the publishers have been fortunate thus far in securing good works.

The book before us is an admirable example of this series, and in one hundred and seventy-two pages contains a concise, clear statement of the subject.

TEXT-BOOK OF MATERIA MEDICA FOR NURSES. By Lavinia L. Dock.
New York and London: G. P. Putnam & Sons, 1890.

This book contains an outline of the source and composition of drugs, their physiological action, symptoms of poisoning and antidotes, and some practical points on their administration, and is intended for the use of nurses in the sick-room. It consists of one hundred and ninety-three pages, and is concisely written, the statements being clear and the arrangement good, following, as it does, that of Brunton and Bruce.

A few mistakes are found in the book, as, for instance, on page 28, alum is called aluminum instead of alumen. On page 42,

ferri oxidum hydratum cum magnesiâ is spoken of as the hydrated sesquioxide of iron and hydrated magnesia, a term which is hardly compatible with the ordinary chemical nomenclature of the present day.

In addition to the Materia Medica, the book contains an appendix, showing the relation of minims to drops in certain medicinal liquids.

A Manual of Weights and Measures, with Rules and Tables. By Oscar Oldberg, Ph.D. Third edition. Revised.
Chicago: W. T. Keener, 1890.

That this little work should have passed through three editions in the space of five years would seem to us in itself a sufficient indication of its worth. The present edition "is supposed to be free from errors, and its value has been enhanced by the addition of several tables."

A Clinical Study of Diseases of the Kidneys. By Clifford Mitchell, A.M., M.D.
Chicago: W. T. Keener, 1891.

Any one who wishes to become an expert in the chemical and microscopical examination of the urine cannot do better than to study the first ninety-seven pages of this book, which deal especially with this subject and their application to the diagnosis of disease. The remainder is occupied with the prognosis and therapeutics of renal diseases, and a description of the different diseases of the kidneys, with their complications and treatment. A number of excellent tables have been introduced throughout the work, which, together with the illustrations, enhance its value. It is well indexed, and in such a manner that the principal references to any subject may be readily found. It is printed in large, clear type, on good paper, and is well bound in cloth.

A Laboratory Manual of Chemistry, Medical and Pharmaceutical. By Oscar Oldberg, Ph.D., and John H. Long, Sc.D. With original illustrations. Second edition, revised and enlarged.
Chicago: W. T. Keener, 1891.

The second edition of this book is a great improvement on the first, which appeared only three years ago. The authors, in the preface, state that typographical errors, as far as discovered, have been corrected, and this appears to have been the case to such an extent that, on careful examination, we have not been able to find any misprints or misstatements in the work.

It is divided into three parts. Part I. contains the chemical elements, with a short, succinct description of the non-metals and the metals, with their tests. Part II. is synthetical chemistry, devoted to inorganic chemistry and preparations with organic acids. Part III. is analytical chemistry, and, in its various means of testing compounds in actual practice, together with volumetric analyses and urinary analysis, is well considered, and condensed into less than one hundred pages. At the end of the book are inserted five plates, consisting of six figures each, in which the principal microscopical ingredients of the urine—normal and abnormal—are well depicted. The work is well calculated to fulfil the object for which it is intended.

A Compendium of Botanic Materia Medica. By Samuel Waggaman, M.D., Ph.D., etc.
Washington, D. C.: W. H. Morrison, 1891.

Professor Waggaman says, "I have merely gleaned from the standard authors the material which I have thus arranged, in what I hope will prove an attractive form. This book is not expected to supply the place of the larger works on the same subject. It is merely intended to simplify the labors of the student, or prove an easy reference for those to whom the subject-matter is already familiar." These objects are fully carried out, and the principles of medical botany are well and simply stated. It will be useful to students of pharmacy, for whom especially it is intended. The pages are rather too closely printed, and the type is small, but fortunately clear.

The Physician's Visiting-List for 1891.
Philadelphia: P. Blakiston, Son & Co.

The Physician's Visiting-List is too well known to require an extended notice. Besides the ordinary visiting-list, it contains an almanac for 1891 and 1892, Marshall Hall's ready method in asphyxia, Sylvester's method in artificial respiration, table of poisons and their antidotes, metric or decimal system of weights and measures, posological tables, and a list of new remedies, aids to diagnosis and treatment of diseases of the eye, and much other matter of importance to the general practitioner. It has also a neat pocket for prescription-blanks and a pencil.

Correspondence.

BERLIN.

(From our Special Correspondent.)

The readers of this journal, if they receive from Berlin only reports of the new treatment of tuberculosis, will be very apt to cry out, "Is there no end to Koch?" I do not intend to review the numerous papers that have already appeared upon the subject, and it is still too soon to pass final judgment on the matter. Virchow's statements at the time of the discussion at the meeting of the Berlin Medical Society have caused, as the newspapers show, much surprise far beyond the boundaries of Germany. He then showed that the injections may produce an increase of the tuberculous process. He has made a longer report on the healing of tubercle, in which he shows that absorption of tuberculous matter cannot occur equally in different parts of the body, since under ordinary conditions tubercle behaves differently in the liver than in the intestines, the larynx, or the lung.

Last evening a discussion was begun at the meeting of the Verein für Innere Medicine on this important matter. Dr. Thorner made the opening remarks, which have been elsewhere published, and which contained nothing of marked importance. Dr. Klemperer, assistant in Professor Leyden's medical clinic, spoke of the alterations in metabolism which occur in patients treated by Koch's method. He found that, after the third week, no increase of the metabolism of albuminates could be proven. The organism, therefore, becomes accustomed to the remedy, which does not happen, so far as we know, in the case of any other toxine.

Surely these experimental results will tend to again increase the trust in the method which had been strongly shaken by Virchow's publications. Never have there been such contrary opinions concerning a remedy as have been given on this question. We hope and wish, in the interest of suffering humanity, that the discussion may progress quietly and without passion, and that the many dark places may be made light. It is especially important at the present time, when so many are using the method, that, on the one hand, there should not be too much enthusiasm, nor, on the other hand, should pessimistic reports frighten physicians and the laity concerning a method that certainly in many cases has given excellent results.

The building in the Charité intended for Koch is so nearly completed that very soon it will be ready to be occupied, and in the mean while the investigations are being carried out under the personal direction of Professor Koch, who, at the present time, is temporarily absent, in the town hospital Moabit.

The police department of Berlin, which has control of all matters of interest to the maintenance of public hygiene, has been led by the discoveries and studies concerning tuberculosis to issue important orders. Henceforth fatal cases of pulmonary phthisis must be reported to the police, while heretofore physicians were required to report all cases of cholera, small-pox, typhoid fever, typhus fever, measles, scarlatina, diphtheria, and puerperal fever, but not phthisis. At the end of the illness everything in the sick-room, including the walls, are properly and thoroughly disinfected. We hope that this measure may be of assistance in overcoming such a terrible enemy to mankind as phthisis, and would recommend other cities to follow the example set by Berlin.

Some investigations have already been made as to the effects of Koch's treatment in cattle affected with tuberculosis, and probably positive and successful results will follow later.

HYPOSULPHITE OF SODIUM AND SILVER IN ATAXIA.

To the Editor of the THERAPEUTIC GAZETTE:

DEAR SIR:—Having a case of locomotor ataxia to treat, and fearing the danger of argyria from the nitrate of silver, I was induced to use the hyposulphite of sodium and silver, thiosulphate of sodium and silver, from a report published by Curci, in the *Medical News*, July 10, 1886, wherein it was claimed this double salt "did not coagulate the albuminoids, is very soluble in water, is not caustic, is diffusible, promptly absorbed by mucous membrane and connective tissue. Its taste is sweet, slightly nauseous. Should be given fasting or hypodermically, by mouth from 5 to 20 centigrammes daily, or 1 to 5 centigrammes daily. Its action is quickly obtained; the danger of argyria is avoided."

My patient was a lady, past middle life,

and her trouble had been slow in coming on. The electric-like pains had been treated as neuralgia and rheumatism; the gastric trouble, as dyspepsia, with pepsin and nux vomica; while the difficulty in locomotion was attributed to the rheumatism. She came under my care early in 1886. The first symptom she then complained of was the difficulty she had just experienced in coming up the stairs, owing to the darkness and some stiffness in her limbs. Though she could walk from her house to the gate at night with considerable certainty, as she was familiar with the locality, yet if she stepped off the walk she would be compelled to sit down, because on the ground she could not get her bearings; that if she did not get back on to the walk, she would be compelled to crawl to the house, for on the ground she felt an uncertainty about her equilibrium. She does not walk on her heels, bringing the sole down with a flap; she walks slightly bent forward, that she may watch where she steps, for a very small obstacle, if stepped upon, is sufficient to cause her to fall. Though she stands with her eyes closed, yet there is a slight swaying motion of the body, such a feeling that she might fall, she does not like to try it. She stands and walks wide; the foot is not carried directly forward with a good knee action, but is held rather stiff and swung around.

She took at first ergot, to relieve some spinal congestion that troubled her mornings. Belladonna, she thought, gave little relief to the bladder-trouble (paralysis of sphincter), and annoyed her by the dryness it caused in the mouth.

She has taken the sodium and silver salt at intervals since 1887 or earlier, as high as 15 centigrammes (2⅓ grains) a day, in all four or five drachms, and has lately commenced on another drachm. Soon after commencing the use of the silver salt her gait improved, and she walked with more ease and spring. She says the silver helped the pains in her limbs, that she could walk better after taking it, but it did not help her bladder-trouble.

Suspension, which she uses at home, she claims greatly helps the bladder-trouble; the only thing that ever did.

With the silver salt and suspension, she says, she can get along very well, if her household work is not too great; that without them she could hardly get along at all.

Very truly yours,

A. RADCLIFFE, M.D.

BUSHNELL, ILL.

Notes and Queries.

A NEW SOURCE OF ARSENIC-POISONING.

In the *Boston Medical and Surgical Journal* for February 19, 1891, DR. WILLIAM N. SWIFT writes that he recently had under his care a child, 6 years of age, who, at the age of two, occasionally suffered from constipation, with offensive breath and coated tongue. He was somewhat salivated, and had at times a few superficial ulcers on the mucous surface of the lips, gums, or tongue. No explanation could be found for this condition, except that he always had a good appetite, and was in the habit, unless watched carefully, of bolting his food. His diet had always been regulated with much care.

In January, 1890, he had the epidemic influenza, and as he was at its onset in one of his debilitated conditions, he was very much pulled down by the illness. During the summer he was in the country, and was perfectly well. When he returned home, he began, in a short time, to look badly. He became anæmic, began to lose weight, and his muscles became soft and flabby. He was constipated. His tongue was coated, and the whole mucous membrane of the mouth became soft and spongy. His breath was offensive. He complained of weakness and occasional cramps in the muscles of the legs when walking. He had to be taken up two or three times at night to prevent him from urinating in bed, and he wet his clothes often during the day.

The plumbing of the house was examined, and found free from any defect. The boy's urine was then analyzed, and arsenic was found. No quantitative test was made, but the amount was considerable. The question was then, What the source of the arsenic might be? The carpet, curtains, and furniture-covering were analyzed, and found free from arsenic. A border and dado of a pictorial paper about the room was known not to contain arsenic. The wall between these was painted a peacock blue, and this paint was found loaded with arsenic. The painter, who had painted the room six years ago, said the color was obtained by mixing Prussian blue and a green. The green pigment undoubtedly contained arsenic. The paint was mixed with lead and oil, and had a smooth, glazed surface.

The patient was sent inland for a change, and he began to improve at once. Since

eliminating the source of poisoning, the boy has been perfectly well.

In looking back on the different attacks that the child had had, during the four years that he had been exposed to the poison, it was noticed that whenever he had been away from home and had come back to this room, the symptoms of debility and stomatitis had developed; but that, after living in the room for some time, he seemed to become used to the poison, and improved somewhat.

The case is interesting, because the evidence seems conclusive as to the cause of the symptoms, the obscurity of the symptoms themselves, and the unusual source of the arsenic, showing that paint should be analyzed, as well as paper and furnishings, in sleeping-rooms.

CARPAINE.

A new alkaloid has recently been detected in papaw-leaves by M. GRESHOFF, of the Chemico-Pharmacological Laboratory at Buitenzorg, in Java. It was obtained by digesting the powdered leaves in spirit acidulated with acetic acid, removing the spirit by distillation, and treating the resulting extract with water so as to leave behind resin and chlorophyll. The aqueous solution was then shaken repeatedly with ether, and carbonate of sodium was added until an alkaline reaction was evident. The precipitate thus obtained was readily soluble in ether, and on evaporation of the ether the "carpaine" was obtained in colorless rosettes of crystals to the extent of about .25 per cent. of the leaves employed. Although the freshly-precipitated alkaloid is readily soluble in ether, when once crystallized it redissolves but slowly, so that the crystals can be purified and rendered perfectly white by washing with a little ether, but the percentage obtained is thus reduced to .15 per cent. On a large scale, the lime and petroleum method gives very good results, about .19 per cent., and would probably be preferred on the score of expense. Comparative experiments made on the young and old leaves, freed from the stalks, show that the old leaves afford when dried .072 per cent. of the alkaloid, and young leaves .25 per cent., and that, on an average, a papaw plant can be calculated to afford thirty grammes of the alkaloid per year from the leaves. The hydrochlorate of carpaine, which contains about eighty-two per cent. of the pure alkaloid, is freely soluble in water. As yet comparatively little is known of the physiological action of the alkaloid. It appears, however, to act more especially upon the heart, slowing its action. The lethal dose for a fowl of five hundred grammes (one pound) weight was found to be about 200 milligrammes (three grains). In a fowl of three hundred and fifty grammes weight, no poisonous symptoms were produced with 50 milligrammes of the alkaloid; with 100 milligrammes, symptoms of poisoning occurred in ten minutes after injection into the breast muscles, but after twenty-five minutes the animal recovered its normal condition. The bird lay on its side, and breathed deeply in a jerky manner, and showed slight convulsive movements of the whole body, but no irritability was noticed. Further observations are necessary to determine the usefulness or otherwise of the alkaloid in medicine. Should it prove of utility, there can be no difficulty in obtaining it in almost unlimited quantity and in a definite crystalline condition. The alkaloid is easily precipitated from its solutions by the alkaloid reagents. The most delicate reaction is with Mayer's reagent,—iodo-iodide of potassium,—which, in a solution of 1 in 300,000, gives a turbidity, and in 80,000 parts an evident precipitate; phosphomolybdate of ammonium has its limit of reaction at 1 in 75,000 parts, picric acid at 1 in 30,000, and chloride of gold at 1 in 25,000. The alkaloid has a bitter taste, which is perceptible even in a solution of 1 part in 100,000.—*Pharmaceutical Journal and Transactions*, December 27, 1890.

ACTIVE PRINCIPLE OF CASTOR OIL.

The identity of the active principle of castor oil has been for many years a subject of much dispute, and the opinion of Buchheim that the castor oil contains no especial ready-formed irritant, but that its action is due to the liberation of ricinoleic acid, which itself possesses the properties of a "scharfer stoff," has been repudiated by Husemann, Boehm, Brunton, Schmiedeberg, and others. On the other hand, the laxative properties of the oil cannot be due to a poison producing gastro-enteritis, contained in the ricinus seeds, and called by Schmiedeberg ricinon, since the latter is destroyed at the temperature of boiling water, under which treatment the activity of the castor oil is not affected, as witnessed by its method of preparation both in the United States and in the East Indies, as well as by direct experiment. By comparison of the

purgative action of ricinoleic acid and its synthetically regenerated glyceride with that of the natural glyceride occurring in castor oil, PROFESSOR HANS MEYER (*Archiv für Experimentelle Pathologie und Pharmakologie*, November, p. 145) has obtained results that substantially support Buchheim's assertion. The ricinoleic acid used in his experiments was prepared as calcium salt from castor oil, and set free after complete purification of the salt by recrystallization from alcohol. The acid possesses a specific gravity of .9451 at 15° C., gives good crystalline barium, zinc, and cadmium salts, and may be converted into the glyceride by heating with glycerin at 280° to 300° C. in a stream of carbonic acid gas. In experiments upon cats and human patients, both the pure acid and the synthetic glyceride appeared to be even more active than the ordinary oil. As, however, the non-activity of the isomeric elaidic acid and elaidin, produced by the action of nitrous acid, still suggested that the active principle of castor oil might be an extremely powerful body not removed from ricinoleic acid by recrystallization, but destroyed by nitrous acid, Professor Meyer carried his investigations further. Arguing that the different physical conditions of the isomerides might account for the difference in purgative action, he administered ricinelaidic acid and ricinelaidin mixed with yolk of egg or milk or dissolved in olive oil. The results showed that the ricinoleic acid had not lost the characteristic property of castor oil through the nitrous acid treatment, but that the apparent non-activity of the elaidic acid is due to its solid condition and higher melting-point (50° C.), which hinder its rapid distribution in the intestines. This is a necessary condition for its successful employment, since the stimulating influence of the ricinoleic acid upon the mucous membrane of the intestines is of short duration and disappears with the absorption of the acid. Castor oil is not, therefore, as other laxatives, cumulative in its action, and from its brief stimulation of the intestines is to be regarded as a most innocuous purge.—*Pharmaceutical Journal and Transactions*, January 31, 1891.

CASES OF POISONING BY BROMOFORM.

Bromoform has been recommended by numerous observers in the strongest terms as a remedy in whooping-cough, but DR. NAUWELAERS (*Revue Mensuelle des Maladies de l'Enfance*, February, 1891) reports a case of poisoning in a child, aged 1 year and 3 months, suffering from whooping-cough, by 2 drops of a solution of 7 drachms to ¼ of bromoform, dissolved in an equal amount of alcohol, and given eight times daily.

The symptoms produced were profound stupor, paleness, coldness, complete muscular relaxation, tracheal râles, feebleness of respiration and circulation, contraction and immobility of the pupil, and insensibility of the cornea. The case proved fatal, and at the autopsy there was found slight congestion of the brain, marked injection of the stomach and duodenum, and great increase in bronchial secretions.

In the *Provincial Medical Journal* for February 2, 1891, is a second case reported by DR. E. SACHS, of a 4-year old child, in whom 3 drops of bromoform were ordered three times a day. In the absence of the mother, the child—doubtless tempted by the sweet taste of the mixture—got at the bottle, and drank what remained in it,—that is, about 15 minims of bromoform. Some time after, the child suddenly turned pale, and, staggering about, was put to bed. When seen by Dr. Sachs it was lying in a seemingly lifeless condition, with fixed dilated pupils, cyanotic lips, imperceptible pulse, and cold extremities. Injections of ether (Pravaz's syringefuls) and the application of a stream of cold water to the chest and back, soon brought the little patient back to consciousness, and the next day it had entirely recovered.

PROPHYLAXIS OF LEAD-POISONING.

M. LAVRAND states, in the *Journal des Sciences Médicales de Lille*, that he has found the administration of the iodide of iron pills of the French Codex, either alone or associated with phosphide of zinc, efficacious in arresting the progress of saturnism in workers in white lead. All the patients presented the earthy complexion characteristic of the initial stage of saturnism. The author found that under this treatment, even though the patients continued to ply their trade, the general health improved and the amount of hæmoglobin increased.—*National Druggist*, February 1, 1891.

CRADINA—A NEW DIGESTIVE FERMENT.

Ten years ago M. Bouchut found a powerful ferment in the juice of the common figtree (*Ficus carica*), and this is now the sub-

ject of a paper (*L'Orosi*, November, p. 364) by DR. MUSSI, who gives a description of the isolation of the substance, and named it *Cradina*, from *krade*, the name given by the Greeks to the part of the fig associated with digestive power. It is insoluble in water, but dissolves readily upon the addition of a trace of acid or alkali, and the solution, placed in contact with moist fibrin, effects complete and true digestion. It contains nitrogen, and in the dry state it forms a friable, semi-transparent, dark yellow, amorphous mass, yielding an amber-yellow powder. In water it swells, but does not dissolve, though upon being shaken it imparts to the liquid a milky appearance. When dissolved by the aid of alkali or acid a concentrated solution is dark yellow, but becomes colorless upon being diluted. Cradina differs from pepsin in maintaining its digestive power in an alkaline liquor, and from papain or papayotin in being insoluble in water, not precipitated from solution by alcohol or lead acetate, and in its activity not being diminished in the presence of hydrochloric acid. In a neutral liquid it is devoid of digestive power and it has no action upon starch.—*Quarterly Therapeutic Review*, January, 1891.

JAMBUL IN DIABETES MELLITUS.

DR. VILLY has devoted his inaugural thesis in Paris this year to a study of the therapeutic value of jambul (*Eugenia jambolana Lamark; Syzygium jambolanum de Candolle*), his studies being made under the direction of Professor Dujardin-Beaumetz, and his results being published in the *Bulletin Général de Thérapeutique* for January 30, 1891. Numerous observations have already been published as to the value of this substance in the treatment of diabetes, but the results have been so contradictory that there must evidently have been some source of error upon the part of one or more of the writers on this subject. Nearly all authors who have studied the question agree in attributing to the seeds alone the mechanism of active properties, while other parts of the plant are either uncertain or without any value whatever. An examination of the literature of this subject also shows the striking difference between the quantities of this substance recommended as a dose by different authors. Some claim that it is only necessary to give fourteen grains to see the diabetes entirely disappear, while others claim to have administered more than seven hundred and fifty grains in twenty-four hours. The remedy does not appear to be entirely without unfavorable after-effects, since cases are on record where its use produced such severe depression as to necessitate its suspension. Nevertheless, the substance cannot be regarded as an active poison, for it is stated that rabbits have received in twenty-four hours their own weight of the powdered jambul seeds without apparently suffering the least disturbance of any kind. In an attempt to explain the asserted action of this substance, one view evidently would suggest itself that it would prevent the formation of sugar from lower carbohydrates, and the statement has been made that the addition of jambul to a mixture of starch and meal, which would naturally give forty-four per cent. of its weight of sugar on the addition of the jambul, only produced nineteen per cent. of sugar. Dr. Villy undertook to investigate the question from this point of view, and, by a number of careful experiments, which he reports in detail, seems to have shown the exact opposite effect is obtained, for he maintains that the jambul, instead of delaying or preventing fermentation of carbohydrates, accelerates it in the most indisputable manner. Dr. Villy takes exception to the deduction of any conclusions of therapeutic value from the experiments reported in previous numbers of the GAZETTE by Graser and Von Mehring, in which jambul succeeded in removing the diabetes mellitus produced by phlorizine, the suggestion being made that a more rational method of testing this would be to produce experimental diabetes through the extirpation of the pancreas, and to then test the action of jambul on the digestion of amylaceous matters. This experiment, however, has not yet been performed, and the author reports three cases of diabetes mellitus occurring in the service of Dujardin-Beaumetz, in the course of which jambul was administered, and from the observations made on these cases the author comes to the following conclusions:

In the first place, the author states that his observations on jambul do not justify the enthusiasm which has hitherto attended its use, and from his point of view the applicability of this vegetable substance is extremely limited. Above all, he lays stress upon the importance of excluding jambul from the treatment of diabetes if the normal regimen is continued, or in such cases the polyuria persists and the glycosuria and albuminuria augment instead of diminishing.

On the other hand, in cases of moderate severity, with or without albuminuria, jambul may apparently prove of some service, provided the regimen be absolutely restricted; and there

can be no doubt that the restriction of diet is the more important measure of treatment, while jambul, like other remedies, is simply accessory to it. Jambul is well supported by the stomach, and may be given in doses of 150 to 200 grains, in divided doses, in twenty-four hours. In cases of severe diabetes, where diet alone will produce any effect, jambul is likewise inefficacious.

AN EARLY ATAXIC SIGN.

Weiss, of Vienna, says that an early symptom of locomotor ataxia is an inability on the part of the patient to walk backward, while as yet, and in other ways, he may be able to walk with firmness and rapidity. Perron, of Bordeaux, has also, as we stated several weeks ago, recently suggested an early diagnostic sign, which is simply a modification of the Romberg test,—namely, causing the suspected ataxic patient to stand upon one leg, instead of two, with the eyes closed. If the patient shows a tendency to fall, it may be inferred that the spinal trouble has begun which will lead on to locomotor ataxia, even if the Romberg test fails, as it not infrequently does in cases that are not well advanced.—*New York Medical Journal*, January 24, 1891.

THE GALACTOGOGUE PROPERTIES OF GALEGA.

At the meeting of the Société de Médecin Pratique, held January 15, 1891, Dr. De la Carrière read a paper, in which he claimed that galega exerted marked influence as a galactogogue in cases where the secretion of milk was diminished (*Le Progrès Médical*, January 24, 1891).

Galega was given in a watery extract, in the dose of from 32 to 64 grains each day, and in almost all cases produced marked augmentation in the secretion of milk within a few days. It is stated that the secretion is not only increased in volume, but that also the solids in the milk are likewise augmented.

RETINOL AS A SOLVENT.

At the meeting of the Société de Médecin Pratique, held January 15, 1891, Dr. Vigier presented a number of preparations in which phosphorus, salol, and creosote were dissolved in retinol (*Le Progrès Médical*, January 24, 1891). He laid great stress on the value of retinol as a solvent for phosphorus. Being unoxidizable, it is admirably suited as a vehicle for the solution of phosphorus, and such a solution remains unchanged indefinitely. So, also, a fragment of phosphorus, if ignited and then plunged into retinol, is instantly extinguished. These preparations of retinol may be used in scrofula, anæmia, chlorosis, muscular paralysis, locomotor ataxia, and, in fact, in any condition in which phosphorus is indicated.

Dr. Vigier also mentions the fact that retinol readily dissolves naphthol, aristol, iodol, codeine, camphor, cocaine, and strychnine.

CHLOROSIS AND ITS TREATMENT.

Dr. Frederick Scholz, of Bremen, has published a remarkable work on chlorosis, the outcome of observations made during the last twenty years. Instead of regarding the deficiency of iron or hæmoglobin, or even that of the red corpuscles, as the primary affection, he states that contraction of the vessels is always present in these cases, as indeed was observed by Bamberger, Rokitansky, and Virchow; and this, he contends, is not to be regarded as a complication due to an altered condition of the blood, but as the primary condition which is followed by the morbid change in the blood. As a matter of fact, the vessels are, he says, too full, or in the condition termed by the older physicians "plethora ad vasa," the blood being—or becoming—abnormally serous. Long ago his attention was struck by the cold and livid condition of the skin in anæmic subjects, and he was led by this to employ hot baths, together with gentle friction, in the treatment, with the view of acting directly upon the skin, so as to improve the vitality and nutrition generally. The success of his first attempts was so marked that he was encouraged to persevere in this line of treatment, and he has since had many opportunities of extending his experience with it. Hot baths diminish the plethora by relaxing the tension of the vascular system, which is high, quickening the circulation, and thus relieving the palpitation, dyspnœa, and other symptoms. In thirty cases where the distress of the patient was very great, Dr. Scholz has gone a step further and supplemented the hot bath by venesection. Paradoxical as this treatment may appear, it was followed by marked benefit, and if the theory of the pathology of chlorosis above mentioned be correct, there can be little doubt that the novel line of treatment practised by Dr. Scholz is justifiable.—*Lancet*, January 24, 1891.

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